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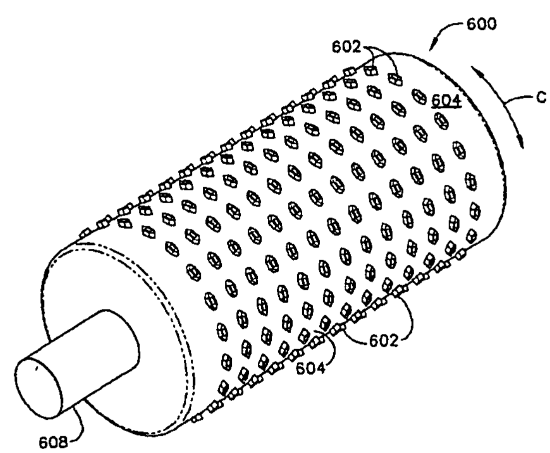
(54) Title: MICROSTRUCTURES FOR DELIVERING A COMPOSITION CUTANEOUSLY TO SKIN USING ROTATABLE STRUCTURES



(57) Abstract: An improved method and apparatus is provided as a system to deliver a composition, preferably a medical or pharmaceutical composition or active, through the stratum corneum of skin, without introducing bleeding or damage to tissue, and absent pain or other trauma. The dimensions and shapes of the microelements are controlled so as to control the penetration depth into the skin. The microelements can be "hollow" such that passageways are created therethrough to allow the composition to flow from a chamber, through the microelements, and into the skin. Alternatively, the microelements can be "solid," and the composition is applied directly to the skin just before or just after the microelements are applied to the skin surface to create the openings in the stratum corneum. Another alternative embodiment uses cylindrical microstructures that are rotatably applied to the skin and which penetrate through the stratum corneum; and which can dispense fluid by various different structures.

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MICROSTRUCTURES FOR DELIVERING A COMPOSITION CUTANEOUSLY TO SKIN USING ROTATABLE STRUCTURES

TECHNICAL FIELD

The present invention relates generally to systems that deliver a composition into skin and is particularly directed to an article of manufacture of the type which is used to deliver a composition cutaneously (or subcutaneously) into skin. The invention is specifically disclosed as a planar array of microelements that are capable of lancing the surface of skin and penetrating the surface of skin to a depth where a composition can be efficaciously applied. The article of manufacture is capable of delivering a composition from a reservoir attached thereto, or the composition can be applied directly to skin and utilized therein in combination with the article of manufacture.

BACKGROUND OF THE INVENTION

Human skin is the largest organ. Aside from the function of regulating skin temperature, the skin's most important function is to serve as an effective barrier against insult of the body by foreign agents, such as toxic substances, microorganisms, and due to mechanical injury. Human skin comprises several layers: the outermost is the stratum corneum, which comprises dead skin cells and makes up a substantial portion of the first protective barrier of the body. Most skin comprises a stratum corneum which is 15-20 layers of dead cells thick (about 10-20 microns in thickness). However, some "durable" skin layers, such as heels or calluses, can comprise a stratum corneum which is from 100-150 microns thick. On average, the skin naturally sheds at least one skin layer each day, and the first one to four layers of skin may be removed without affecting the protective nature of skin or the health thereof. In fact, removing up to four (4) layers of the stratum

corneum may provide a skin surface area onto which make-up may be more uniformly applied and once applied has a more aesthetically pleasing appearance.

Penetration of the outer layers of skin to deliver a pharmaceutical composition is a widely held practice. Typically injections of pharmaceuticals are affected by subcutaneous delivery, intramuscular delivery, as well as intravenous delivery. Less invasive procedures have now been developed and are widely utilized. Among these "topical" applications are patches, which are used to provide slow release of a composition, such as air and motion sickness compositions, or cigarette smoking abatement compositions. However, these patch delivery systems rely on formulations that can carry the active ingredients across the skin barrier into the blood stream. Therefore, formulation and dosing limitations may provide an encumbrance to delivery of a medication or skin benefit composition via patch.

There is, therefore, a long felt need for an article of manufacture that can be used to deliver a composition cutaneously (or subcutaneously) to skin. Specifically, there is also a need for article that is capable of lancing the surface of skin or is capable of penetrating the surface of skin to a depth where a composition can be efficaciously applied.

One solution to the above-noted long felt need is a "patch" that contains a plurality of microneedles, in which each individual microneedle is designed to puncture the skin up to a predetermined distance, which typically is greater than the nominal thickness of the stratum corneum layer of skin. Using such microneedle patches provides a great benefit in that the barrier properties of the skin can be largely overcome, while at the same time the microneedles can be painless and bloodless if they are made to not penetrate through the epidermis.

One problem with microneedles is that, first they require a direct pushing motion against the skin, which may or may not be of sufficient force to penetrate completely through the stratum corneum and, second even when they do penetrate the stratum corneum, their efficiency of compelling a fluid (such as a liquid drug or other active) though their relatively tiny openings is not great (these microneedles are usually quite small in diameter). It would be an improvement to provide a microstructure (e.g., in the form of a hand-held patch) that can provide a greater efficiency of flow for some type of

fluidic compound through the stratum corneum, and to make it possible for the microstructure to penetrate the outer skin layers (e.g., the stratum corneum) by a sliding, rubbing, or rolling motion that is essentially parallel to the skin surface, rather than perpendicular to the skin surface. The sliding/rubbing/rolling motion allows each microelement protruding from the substrate (or base) of the microstructure to make multiple slits or cuts in the outer layers of the skin, which increases the permeability of the skin (i.e., it reduces the skin's barrier properties) at that local area.

SUMMARY OF THE INVENTION

Accordingly, it is an advantage of the present invention to provide a method and apparatus that can deliver either a benefit to human skin or deliver a composition cutaneously into skin.

It is another advantage of the present invention to provide an article of manufacture that is capable of lancing the surface of skin, or of penetrating the surface of skin to a depth where a composition can be efficaciously applied.

It is a further advantage of the present invention to provide an article of manufacture that is capable of repeatedly penetrating the skin to a predetermined depth, thereby providing a means for delivering a composition to the sub stratum corneum layer.

It is yet another advantage of the present invention to provide a rotating microstructure that includes a plurality of microelements that can penetrate the skin through at least the stratum corneum layer, and to dispense a fluid through the openings created in the stratum corneum.

It is still another advantage of the present invention to provide a microelement structure in which there are two half-microelement structures or portions that are spaced-apart from one another, and in which an opening in a substrate is formed therebetween.

Additional advantages and other novel features of the invention will be set forth in part in the description that follows and in part will become apparent to those skilled in the art upon examination of the following or may be learned with the practice of the invention.

To achieve the foregoing and other advantages, and in accordance with one aspect of the present invention, a rotatable microstructure apparatus is provided, which comprises: a roller structure which includes a curved substrate and a plurality of microelements affixed upon a first surface of the substrate; the plurality of microelements being of predetermined sizes and shapes so as to penetrate a stratum corneum layer of skin when the microstructure apparatus is placed upon the skin and rolled over the skin in at least one predetermined direction.

In accordance with another aspect of the present invention, a method for reducing the barrier properties of skin is provided, in which the method comprises the following steps: (a) providing a rotatable microstructure having a curved substrate and a plurality of microelements that protrude from the curved substrate by at least one predetermined protrusion distance; and (b) placing and rolling the rotatable microstructure on a surface of skin, wherein the at least one predetermined protrusion distance is sufficient so that many of the plurality of microelements penetrate a stratum corneum layer of the skin.

In accordance with yet another aspect of the present invention, a microstructure apparatus is provided, which comprises: a plurality of microelements affixed upon a surface of a substrate, the plurality of microelements being of sizes and shapes so as to penetrate skin when placed into contact therewith; wherein at least one of the microelements comprises: (a) two half-structures that are spaced-apart from one another, and (b) an opening in the substrate surface, the opening being positioned between the two half-structures.

The present invention relates further relates to embodiments of the article of manufacture which allows sustained cutaneous delivery of a enhancing composition, pharmaceutical composition, or the like.

Still other advantages of the present invention will become apparent to those skilled in this art from the following description and drawings wherein there is described and shown a preferred embodiment of this invention in one of the best modes contemplated for carrying out the invention. As will be realized, the invention is capable of other different embodiments, and its several details are capable of modification in various, obvious aspects all without departing from the invention. Accordingly, the drawings and descriptions will be regarded as illustrative in nature and not as restrictive.

All percentages, ratios and proportions herein are by weight, unless otherwise specified. All temperatures are in degrees Celsius ($^{\circ}C$) unless otherwise specified. All documents cited are in relevant part, incorporated herein by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings incorporated in and forming a part of the specification illustrate several aspects of the present invention, and together with the description and claims serve to explain the principles of the invention. In the drawings:

Figure 1 is a plan view of an array of microelements that are pyramidal in shape, as constructed according to the principles of the present invention.

Figure 2 is a perspective view of one of the pyramidal microelements of Figure 1.

Figure 3 is an array of pyramidal microelements as according to Figure 1, with the addition of through-holes in the substrate, and channels along the sides of the microelements.

Figure 4 is a perspective view of the pyramidal microelements of Figure 3.

Figure 5 is a plan view of an array of microelements that have an overall cubic rectangular shape, as constructed according to the principles of the present invention.

Figure 6 is a perspective view of one of the cubic rectangular microelements of Figure 5.

Figure 7 is a plan view of an array of the cubic rectangular microelements of Figure 5 with the addition of through-holes in the substrate.

Figure 8 is a perspective view of one of the cubic rectangular microelements of Figure 7.

Figure 9 is a plan view of an array of wedge-shaped microelements, as constructed according to the principles of the present invention.

Figure 10 is a perspective view of one of the wedge-shaped microelements of Figure 9.

Figure 11 is a plan view of an array of the wedge-shaped microelements of Figure 9 with the addition of through-holes that penetrate through the microelement and through or into the substrate.

Figure 12 is a perspective view of one of the wedge-shaped microelements having through-holes of Figure 11.

Figure 13 is a plan view of an array of wedge-shaped microelements of Figure 9, in which a through-slot is located in the microelements, which penetrates through or into the substrate.

Figure 14 is a perspective view of one of the wedge-shaped microelements having the through-slot of Figure 13.

Figure 15 is a plan view of an array of microelements having an elongated triangular shape, as constructed according to the principles of the present invention.

Figure 16 is a perspective view of one of the elongated triangular microelements of Figure 15.

Figure 17 is a plan view of an array of the elongated triangular microelements of Figure 15 with the addition of through-holes in the substrate, and elongated channels along the surfaces of the triangular microelements.

Figure 18 is a perspective view of one of the elongated triangular microelements of Figure 17.

Figure 19 is a plan view of an array of triangular-shaped wedge microelements that are grouped in closely-spaced arrangements, as constructed according to the principles of the present invention.

Figure 20 is a perspective view of one of the closely-spaced triangular wedge microelements of Figure 19.

Figure 21 is a plan view of an array of arcuate-shaped microelements with wedged tips, as constructed according to the principles of the present invention.

Figure 22 is a perspective view of one of the wedge, arcuate-shaped microelements of Figure 21.

Figure 23 is a plan view of an array of the wedge, arcuate-shaped microelements of Figure 21 with the addition of through-holes that penetrate through the microelement and through or into the substrate.

Figure 24 is a perspective view of one of the wedge, arcuate-shaped microelements of Figure 23 having through-holes.

Figure 25 is a plan view of an array of the wedge, arcuate-shaped microelements of Figure 21 in which a through-slot is located in the microelements, which penetrates through or into the substrate.

Figure 26 is a perspective view of one of the wedge, arcuate-shaped microelements of Figure 25 having the through-slot.

Figure 27 is a perspective view of one of the "straight" wedge-shaped microelements 102 as it makes a slit or cut in skin.

Figure 28 is an elevational view in partial cross-section of a wedge-shaped microelement of Figure 10, in which the side walls are perpendicular with respect to the substrate plane.

Figure 29 is an elevational view in partial cross-section of a wedge-shaped microelement similar to that of Figure 10, in which the side walls have an angular relationship that is not perpendicular with respect to the substrate plane.

Figure 30 is an elevational view in partial cross-section of an array of microelements similar to those found in Figure 23, with the addition of through-holes or passageways to a reservoir structure below the main substrate.

Figure 31 is a plan view of a microelement array as seen in Figure 10, with the addition of a non-woven backing material that is laminated to the original substrate.

Figure 32 is a plan view of a plurality of microelement strips that are laminated onto a non-woven backing.

Figure 33 is an elevational view in partial cross-section of a microelement array as seen in Figure 10, showing further details of the substrate and non-woven backing.

Figure 34 is perspective view of a microstructure in the shape of a cylindrical roller, as constructed according to the principles of the present invention.

Figure 35 is an enlarged perspective view of one of the microelements used in the microstructure of Figure 34.

Figure 36 is perspective view of a microstructure in the shape of a cylindrical roller, as constructed according to the principles of the present invention.

Figure 37 is an enlarged perspective view of one of the microelements used in the microstructure of Figure 36.

Figure 38 is perspective view of a microstructure in the shape of a cylindrical roller, as constructed according to the principles of the present invention.

Figure 39 is an enlarged perspective view of one of the microelements used in the microstructure of Figure 38.

Figure 40 shows several more-detailed views of the microelement depicted in Figure 39.

Figure 41 illustrates two different views of an alternative microelement that can be used with the microstructure of Figure 38.

Figure 42 illustrates three views of an alternative microelement that can be used with the microstructure of Figure 38.

Figure 43 is a side view in cross-section of a hand-held rolling microstructure apparatus for dispensing a fluid into skin, that has a hand-operated pushbutton for dispensing the fluid, as constructed according to the principles of the present invention.

Figure 44 is a perspective view of a roller assembly that contains a cylindrical microstructure placed upon skin for dispensing a fluid into skin, as constructed according to the principles of the present invention.

Figure 45 is a side view in cross-section of an alternative embodiment of a hand-held rolling microstructure apparatus for dispensing a fluid into skin, as constructed according to the principles of the present invention.

Figure 46 is a side view in cross-section of an alternative embodiment of a hand-held rolling microstructure apparatus for dispensing a fluid into skin, which uses a traveling nut to dispense the fluid, as constructed according to the principles of the present invention.

Figure 47 is a side view in cross-section of an alternative embodiment for dispensing fluid from a reservoir using a traveling nut, as constructed according to the principles of the present invention.

Figure 48 is a side view in cross-section of a rotatable cylinder with microelements that dispenses fluid from the interior reservoir of the cylinder using a dosing paddle, as constructed according to the principles of the present invention.

Figure 49 is a side view in cross-section of an alternative embodiment of a rotatable cylindrical microstructure that can dispense fluid from an interior reservoir,

which uses a planetary gear set to move a wiper or dosing paddle, as constructed according to the principles of the present invention.

Figure 50 is a perspective view of the cylindrical rotatable dispenser of Figure 49.

Figure 51 is a perspective view of a cylindrical microstructure that includes two sets of threads for tightening the skin as it is being penetrated by microelements on the surface of the microstructure, as constructed according to the principles of the present invention.

Figure 52 is a side view in partial cross-section of the rotatable cylindrical dispensing apparatus of Figure 51.

Figure 53 is a perspective view of a microelement that comprises two pyramidal half-structures, as constructed according to the principles of the present invention.

Figure 54 is a top view of the microelement of Figure 53.

Figure 55 is a side view in partial cross-section of the microelement of Figure 53.

Figure 56 is a perspective view of a microelement that comprises two half-structures having wedge-shaped individual elements, as constructed according to the principles of the present invention.

Figure 57 is a top view of the microelement of Figure 56.

Figure 58 is a side view in partial cross-section of the microelement of Figure 56.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Reference will now be made in detail to the present preferred embodiment of the invention, an example of which is illustrated in the accompanying drawings, wherein like numerals indicate the same elements throughout the views.

The present invention relates to cutaneous delivery of a composition to the body by way of an article of manufacture, which controllably penetrates the outside layers of human skin. The present invention further relates to an embodiment wherein the article of manufacture remains attached to the skin surface and is capable of protracted delivery of a composition, or protracted sampling of a biological fluid, such as interstitial fluid.

For the purposes of the present invention the term "cutaneous delivery" is defined as "a composition which is controllably delivered to human skin by an article of

manufacture wherein the article of manufacture is capable of penetration of the skin layer to a finite depth without producing concomitant trauma." The words cutaneous and subcutaneous are essentially interchangeable terms as used herein. The term "trauma" is defined herein as "pain associated with the application of the article of manufacture to the surface of skin, bleeding, bruising, swelling, damage to skin areas, and the like."

Self-administration of drugs is a necessity for many individuals. Aside from topically applied medication treating skin itself, most medications are self-administered orally. However, there is wide recognition that some categories of formulations, such as pharmaceutical formulations, are best administered directly into body tissue, for example, intravenous (IV), intramuscular (IM) injections. When applying both IV and IM injection techniques, there are a number of considerations. For example, the skill of administering person, the will of a patient to self-administer an injection, or the effectiveness of the patient's self-delivery must be considered when prescribing a treatment plan.

These issues can be held in abeyance and compositions, pharmaceutical or otherwise, can be delivered routinely to humans without the concerns of pain, swelling, trauma, or lack of compliance by the patient. In addition, the inconvenience of storing and re-supplying of syringes, swabs, and the like are made unnecessary by the systems and principles of the present invention.

The stratum corneum of skin comprises layers of dead skin cells, which are part of the body's protective outer layer. This outermost layer of skin cells can have a nominal thickness of from about one hundred (100) microns to about 250 microns for thick, durable skin areas, such as calluses, whereas normal, "thin" skin may comprise from about ten to about fifteen microns (10-15) thickness for its stratum corneum. One aspect of the present invention relates to the penetrating or piercing the stratum corneum. The articles of manufacture described herein can be configured to provide various sizes and shapes of penetrating microelements. One way this is achieved is by adjusting the configuration of the microelements and/or the distance from which the distal end of the microelements protrude from a particular base element.

By adjusting the configuration of the penetrating microelements, not only is the depth of skin penetration modulated, but also the type of penetration can be adjusted. For example, the articles of manufacture of the present invention may have hollow or grooved

penetrating microelements, which can serve as passages through which a substance may flow. These passages allow for transport of a composition to the skin, for example, a pharmaceutical, preferably without bleeding, pain, or other associated trauma. The terms "microelement" and "penetrating microelement" are interchangeable as used herein.

Articles of Manufacture:

The articles of manufacture of the present invention comprise a base element (or "substrate") onto which is affixed or deposed a plurality of microelements. The following is a description of the base element and corresponding microelements.

Base Element:

The articles of manufacture of the present invention comprise at least one base element having a first side and a second side. Onto the first side are affixed the penetrating microelements as described hereinbelow. Aside from providing a template or base structure onto which the microelements are affixed, the second side, or reverse side, may in turn comprise a handle or other means by which the article of manufacture can be held. In another embodiment, a substance can be deposed upon the second side, which allows the user to grasp, hold, or otherwise control the motion of the article using only the fingertips. The use of a material to provide a tactile surface is especially compatible for embodiments wherein the base element comprises a thin, flexible material, such as paper or polymeric sheets. One embodiment of the present invention includes base elements which comprise flexible sheets, and the thickness of the sheets is determined by the desired degree of flexibility. The flexible sheets are typically rigid enough to provide a template upon which the microelements can be affixed, but which are easily deformed to fit the contours of the skin surface.

The base elements of the present invention may have any shape or configuration. For example, one embodiment relates to circular base elements, while another embodiment relates to rectangular base elements having a width and a length. For such articles of manufacture that comprise microelements having a "microelement angle" less than 90° as defined hereinbelow, rectangular base elements will have a left edge and a right edge. The right edge of the base element is defined herein as the edge along the

right side of the base element when the second side of the base element is facing down (away from the observer) and the first side is facing the observer. The left edge is oppositely defined herein.

In another embodiment of the present invention, the second side may have a reservoir (or chamber) attached thereto (or constructed therewith) which contains a flowable (or "fluidic") composition, or at least one reservoir or chamber for receiving material (e.g., interstitial fluids) removed from skin. For embodiments of this type, it is an option to modify the base element to comprise a plurality of hollow elements, or to provide channels or pore openings along with solid microelements. Such hollow elements or channels would ostensibly provide a means for a deliverable material or removable material to flow from the first side of the base element to the second side, or vice versa. The hollow elements can also be in register with a hollow element, channel, hole, or other passageway which modifies the microelements as described hereinbelow in a manner that allows a flowable composition to be delivered from the reservoir through a hollow element in the base element, through a tube or channel of the microelement, and into skin.

For purposes of the present invention, the terms "fluid" or "fluidic" have a meaning that includes flowable liquids, flowable gases, relatively low-viscosity creams, flowable solutions that may contain solid particles, and the like. A "fluidic compound" or "fluidic material" specifically includes such liquids, gases, and solutions; these compounds or materials may comprise an active, a drug, or a skin conditioner, or other useful composition of matter; alternatively, the term "fluidic compound" can represent at least two actives, drugs, or the like, including both a biological active and a chemical active (in a single fluidic compound).

Penetrating Microelements:

The articles of manufacture of the present invention further comprise a plurality of penetrating microelements, which are affixed to the first side or first surface of the base element. The "proximal end" of the microelement is defined herein as "the penetrating microelement end, which is affixed to or in register with the base element." The "distal end" of the penetrating microelement is defined herein as "the penetrating microelement

end which comes into contact with skin, and which is the opposite end of the microelement from the proximal end." The term "penetrating microelement" is defined herein as "an appendage for contacting skin which extends from the first side of the base element and is affixed thereto (or protrudes therefrom) at an attachment angle." The term " penetrating microelement" refers to the entire element which contacts the skin and includes not only the appendage itself, but the attachment angle, any hollow elements or grooves, the density of the microelements as measured in the number of appendages per square centimeter, and any pre-disposed composition of matter on the microelement surface.

The general purpose of the penetrating microelement is to lance, cut, or otherwise open the outer layers of skin to a predetermined depth or configuration in order to deliver a composition. In one embodiment of the present invention, the penetrating element is durable and can, therefore, be reused; however, embodiments which are disposable are also encompassed by the present invention, and do not reqqire cleaning or sterilization after use.

For the purpose of the present invention the term "lancing" (or "cutting") is used herein to define the use of a "penetrating element that has a predetermined height and width, wherein the skin is cut to a predetermined limited depth and a predetermined slit opening width as even pressure and sliding force is applied by the microstructure patch to the skin surface by the user, in which the depth and slit opening width of the cut made by the microelement directly corresponds to the skin healing time (i.e., the time required for the skin to recover its barrier properties)." Lancing elements are typically use to penetrate the easily cut tissue or tissue which is mechanically damaged, for example, an infected area of the skin which is tender to the touch or which has scab formation proximal to the area to be treated. In addition, penetrating elements which "lance" may be more suitable for articles of manufacture that are used to treat skin grafts or tissue damaged by heat, such as in first degree or second degree burns.

The term "lancing" typically connotes a single effective stroke, whereas a "sawtooth" penetrating element is used to penetrate skin that is more durable and resistant to mechanical pressure, although such sawtooth motion can also be used on normal "thin" skin. Embodiments of the present invention that employ sawtooth motions can be used in

"durable areas" of the skin, and include the heel and toe areas, as well as, calluses, corns, and the like. Virtually all embodiments of the present invention can be used with either a single penetrating stroke, or with a back and forth (or "sawtooth") motion against the surface of skin.

As used herein, the term "rubbing" represents an action by which one of the microstructures of the present invention is placed upon skin and moved along the surface of the skin. The rubbing action can be achieved manually, or by using a device. In other words, the microstructure can be held by hand and manually rubbed against the skin, or the microstructure can be placed on a mechanical device that will, in turn, be used to move (or rub) the microstructure upon the surface of the skin.

The term "skin" is defined herein as "animal skin, including human skin, plant skin or surfaces, and even other biological structures that may not have a true "skin" organ, such as tissue samples of either plant or animal origin."

For the purposes of the present invention, the term "affixed" as it relates to attachment of the microelements to the base element is defined as "held permanently to the first side of the base element." Affixed microelements are neither removable nor detachable. The microelements of the present invention, as it relates to the term "affixed," can comprise any suitable embodiment. For example, the microelements and base element may comprise a single uniform composition or the microelements may be extruded from the material comprising the first side.

Alternatively, and in a separate embodiment, the microelements may be applied to the base element in a separate operation or manufacturing step, such as lamination to a non-woven substrate. Therefore, the microelements can be fashioned and applied in any manner the formulator desires which achieves the desired microelement density or configuration, or which achieves the desired penetrating properties. Other suitable microelement configurations include those described in United States Patent Applications: U.S. Serial Number 09/580,780, U.S. Serial Number 09/580,819, and U.S. Serial Number 09/579,798 all filed May 26, 2000; U.S. Serial Number 09/614,321 filed July 12, 2000 all of which are commonly-assigned to The Procter & Gamble Company, and which are incorporated herein by reference.

For the purposes of the present invention the term "microelement density" is defined herein as "the number of microelements per square centimeter of base element surface."

The appendages that comprise the microelements may be of any configuration that is capable of providing the desired skin penetration necessary to deliver a composition or treatment. One embodiment of the present invention relates to a plurality of appendages in the form rod-shaped appendages that are either circular or elliptical, perhaps having a uniform circumference along the entire length. Planar appendages include cubes or cubic rectangles (or open boxes) wherein the length and width are uniform (but not necessarily equal to one another) throughout the height of the appendage and the distal end comprises a plane, such as a square, rectangle, or trapezoid, in which the plane is parallel to the base element or at an angle thereto. Wedge-shaped appendages have a rectangular proximal base that tapers to a line segment, which preferably has the same length as the length of the rectangular base. Some wedge-shaped appendages may have an inverted appearance. Pyramidal appendages may comprise bases which have three or four sides at the proximal end base, and which taper to a point or rounded top at the distal end. Alternatively, the wedge-shaped appendages may have a triangular section removed therefrom that acts to facilitate the removal of skin hair follicles. The appendages of the present invention may also be coiled or otherwise arcuate, having any number of turns from the proximal end to the distal end.

One embodiment of the present invention relates to a plurality of lancing elements arranged laterally across the front edge of the base element. Sawtooth-like embodiments may have the "teeth" varied in a variety of ways, for example, the size (height) of the teeth, the spacing between teeth, and whether the ends of the teeth are tapered to a more narrow width. Other penetrating elements include square or rectangular posts, blades (circular and straight), straight or curved wedges, or pyramidal-, cylindrical-, cube-, and star-shaped elements.

For the purposes of the present invention the term "penetrating element angle" is defined as the "angle at which the appendage of the penetrating microelement protrudes from the base element." For example, a microelement, which is affixed perpendicular to the base element, has a penetrating element angle of 90°. The microelements of the

present invention can be affixed to the base element at any angle from about 30° to about 90° (perpendicular). However, if the direction of use of the article of manufacture is not symmetrical, the microelements can be affixed to the base element at any angle from about 30° to about 150°. In addition, microelements which are not perpendicular to the base element may be angled toward any edge of a rectangular or square base element, or be perpendicular to the tangent of any point along the circumference of a circular base element.

The penetrating microelements of the present invention may also comprise hollow elements or contain grooves. Hollow elements are typically disposed along the longitudinal axis of the appendage portion of the microelement and are in register with a corresponding hollow element or passageway at the base element. Grooves or indented elements occur along the surface of an appendage and serve, like hollow elements, to provide a means for a solution to be delivered into the fissures created by the penetrating elements. Embodiments having at least one reservoir or chamber can deliver a fluidic compound into the skin.

The microelements of the present invention may range from absolute rigid (inflexible) to flexible. For the purposes of the present invention, the term "flexible" is defined herein as "during use against skin, the distal end of an appendage is bent or deformed up to 90° from the microelement angle as defined herein above." A perpendicular appendage which is bent 90° is therefore parallel with the base element. An appendage having a microelement angle of 45° can be deformed or bent to an angle of 135°. It will be understood, however, that the penetrating microelements that cut into skin, as discussed below, are typically non-rigid in nature.

The penetrating elements of the present invention may have a protrusion distance of up to 1000 microns from the surface of the base element. The term "protrusion distance" is defined herein as "the distance from distal end of the penetrating microelement along a line parallel to the base element." For perpendicular microelements the length of the appendage and the protrusion distance are equivalent. A microelement having a microelement angle, for example, of 30° will have a protrusion distance equal to one half the length of the appendage.

One embodiment of the present invention relates to microelements having a protrusion distance of about 1-1000 microns. Another embodiment relates to protrusion distances of about 1-200 microns. Further embodiments encompass penetrating microelements wherein the appendages have protrusion distances from about one to about twenty (1-20) microns, whereas other embodiments include protrusion distances of from about five to about twenty (5-20) microns and from about four to about twenty (4-20) microns, as well as embodiments from about four to about ten microns (4-10). Other embodiments comprise no range of protrusion distances but have discreet distances, for example, a 4-micron embodiment, a 5-micron embodiment, a 10-micron embodiment.

The penetrating microelements of the present invention may comprise an appendage which has flexible elements and rigid elements such as, for example, an appendage which has a rigid portion extending from about the middle of the element to the proximal end and a flexible portion extending from about the middle of the element to the distal end. Articles of manufacture which are composites of several materials may comprise a thin flexible base element onto which are deposed rigid, inflexible penetrating elements. As noted above, most of the penetrating microelements described herein will be rigid in nature.

The articles of manufacture of the present invention may comprise a multitude of arrays, each array comprising the same or different types or sizes of microelements, in which the various attributes of the microelements, including microelement density, appendage type, microelement angle, hollow elements vs. solid elements with or without grooves, degree of flexibility, protrusion distance, etc. may vary from array to array or within a single particular array. For the purposes of the present invention the term "array" is defined as "multiple microelements in a pattern."

In some cases, certain array elements collectively may be separated from another array by a distance which is greater than the distance between the microelements which comprise the first array. In other cases, arrays may contain different types of microelements which all have the same spacings. The distance between microelements along the edge of two separate and distinct arrays may be greater than the distance between two microelements, which are members of the same array. Alternatively, several different microelement shapes or protrusion sizes may exist in a single array in which all

individual elements are spaced-apart from one another in a consistent manner throughout the entire structure.

The microelements preferably have a length and shape that will tend to penetrate entirely through the stratum corneum layer by a cutting ("lancing"), slitting, or plowing motion. The characteristic of the microelements to cut and penetrate entirely through the stratum corneum is further enhanced by directing the user to move the "patch" or microstructure substantially in only one direction (or substantially along a single line that represents a back and forth direction), so that the "sharper" edges of the microelements tend to cut or plow into the skin upper layers. This allows a liquid or cream-like substance (i.e., a fluidic compound) to be placed into the slits or cuts made in the stratum corneum, and greatly enhances the amount of such fluid or cream (e.g., an active, drug, or other compound) to enter through the stratum corneum. Furthermore, so long as the penetration depth is properly controlled (which is accomplished by providing microelements having proper shapes and lengths), the skin heals very quickly; in some circumstances, the skin's barrier properties recover in less than two hours!

The methodologies for using "solid" microelements are expected by the inventors in two main embodiments: (1) first to cut (or "lance") the skin using the microstructure (or patch), then apply a fluidic material (such as an active) onto the same skin area after withdrawing the microstructure patch, and the fluidic material will tend to penetrate into the stratum corneum through the slits just previously made; or (2) first to apply the fluidic material onto the skin and then place the microstructure patch upon the same skin area and out (or lance) the skin, thereby assisting (or forcing) the fluidic material to penetrate through the stratum corneum.

A further methodology for use involves microelements having holes or slots therethrough, or through-holes in the substrate adjacent to the microelements. In this embodiment of use, the skin is cut ("lanced") and a fluidic material is applied through the holes/slots in a single procedural step. Of course, the skin must first literally be slit or cut through its stratum corneum layer before the fluidic material can flow through the slits formed therein, but this essentially can occur virtually simultaneously while the user makes a single back and forth set of movements (or perhaps even a single stroke in only one direction would suffice in certain physical configurations of microstructures). A

reservoir of some type to hold the fluidic material would be required as part of the microstructure patch in this methodology, although there are variations available as to the exact construction of such a reservoir, as described below.

Referring now to the drawings, Figure 1 illustrates a microstructure array generally designated by the reference numeral 10 containing multiple microelements 12 that are situated on a base or substrate 14. In Figure 1, each "column" of microelements 10 is offset from the next, adjacent column of similar microelements. However, each of the columns could be made to be identical to one another, if desired, and the offset could be removed. Alternatively, there could be several columns with various offsets before the microelement pattern repeats, or the offsets could be substantially random so that there is no repetitive pattern.

Figure 2 illustrates in a magnified view one of the microelements 12, which has the appearance of a four-sided pyramid. Each side wall of the pyramid is designated at the reference numeral 20, and the seam or "corner" between sides is located at the reference numeral 22. The pyramid's peak is illustrated at 24, and the base line of each of the sides is located at 26, where it meets the substrate 14.

This array 10 of microelements is very useful in penetrating the stratum corneum layer of skin by forming it into a patch that can be held by a human hand, and placed against a particular area of skin and then rubbed in a straight back and forth motion (or perhaps in a circular motion, if desired). When the patch or array 10 is rubbed against the skin, the microelements 12 will tend to penetrate into the dead skin cells, and will do so with a lateral, sliding motion (that is substantially parallel to the skin surface) instead of using a pushing or thrusting motion (that is basically perpendicular to the skin surface).

The array or patch 10 will correctly perform its functions of penetrating through the stratum corneum without regard to the direction of movement of the patch 10 with respect to the orientation of the individual microelements 12. In other words, these microelements 12 are omnidirectional in operation, and all directions are preferred, or even "predetermined." Other embodiments of the invention described below are not omnidirectional, and instead are unidirectional or bi-directional in nature with respect to the orientation of their individual microelements.

The microelements will cut into the skin to a predetermined "penetration depth," which will be controlled by (and probably substantially equivalent to) the "protrusion distance" of the microelements 12. Other embodiments of the present invention, as described below, will function in a like manner.

Another feature of the microstructure 10 is its capability for use in applying a conditioner or other type of compound that is in the form of a liquid or a cream. Just after the microstructure patch 10 has penetrated an area of skin, the stratum corneum will have numerous slits or cuts therewithin, which significantly reduces (at least temporarily) the skin's barrier properties. A fluidic compound can now be applied to the skin, which will much more readily make the journey into the epidermal layer. The fluidic compound could be some type of drug or other active, if desired. The other microstructures described below will also lend themselves well for this type of topical application of a fluidic compound to penetrate into skin.

A further feature of the microstructure 10 is its capability for a compound to be applied onto the substrate 14 and/or microelements 12 in advance of its placement against an area of skin. When the microstructure patch 10 is placed onto the skin, it will impart some of this compound onto the same area of the skin that is being penetrated—this will essentially occur simultaneously. The other microstructures described below will also lend themselves well for this type of simultaneous delivery of a fluidic compound to the same area of skin that is being penetrated. Of course, the embodiments described below which include through-holes in the substrate (e.g., see Figures 3 and 4) may not be the first choice for this methodology of composition delivery, but such devices certainly could be used in this manner, if desired. The compound that is pre-applied to the surface of the microstructure 10 could be placed either by the user, or at the time of manufacture of the microstructure 10.

Figure 3 illustrates a similar microelement array, generally designated by the reference numeral 30, in which through-holes and channels are added. The base or substrate 34 includes a plurality of through-holes 36 that are positioned proximal to the base of the individual pyramidal microelements 32. These through-holes 36 can either penetrate through the entire substrate 34, or can penetrate partially into the substrate and

connect to passageways that may run in a direction perpendicular to the through-holes, and make common connections between many of the through-holes.

On Figure 4, further details are visible, in which the side walls 40 of the pyramidal microelement 32 are seen to have grooved channels 38 which connect to the through-holes 36. The edges of the side walls 40 are at reference numeral 42, the individual base lines of the pyramid are at 46, and the peak of the pyramid is at 44.

On Figures 3 and 4, the array 30 of multiple pyramidal structures at 32 all have a through-hole adjacent to each side of the pyramid. Of course, there could be fewer through-holes 36 per pyramidal microelement 32, if desired. Alternatively, some of the pyramidal microelements 32 in the array could have no adjacent through-holes, if desired. Such microelements (or others in the array) could also forego the channels 38.

The structure of Figures 3 and 4 is useful to perform a simultaneous penetration and drug delivery step. While the array or "patch" 30 is rubbed along the skin, the skin cells of the stratum corneum will be cut, lanced, or slit (or otherwise penetrated) by the individual pyramidal microelements 32, which will prepare the skin for any type of fluidic compound that will then be "injected" through that area of skin surface. A capillary force will work to the advantage of delivering a drug or other active. Of course, mechanical pressure or iontophoresis could be used to assist in the delivery, for example.

It will be understood that instead of delivery of a fluidic compound such as a drug into the skin, the microstructures disclosed in Figures 3 and 4 could be used to sample an interstitial fluid, for example. In that event, the fluid flow would of course be in the opposite direction through the through-holes 36, and would subsequently be directed to a collecting reservoir or chamber, as for example, is described below.

Similar to the patch 10, the array or patch 30 will correctly perform its functions of penetrating the skin cells of the stratum corneum without regard to the direction of movement of the patch 30 with respect to the orientation of the individual microelements 32. In other words, these microelements 32 are omnidirectional in operation, and all directions are preferred, or even "predetermined."

Another potential use of the array or patch 30 is to attach the entire microstructure patch to skin for an relatively lengthy time interval, and thereby provide a capability for protracted delivery of the fluidic compound into the epidermis, using the cuts or slits that

were formed during the previous rubbing procedure. It also would be possible to sample biological fluids for a prolonged time interval by attaching the microstructure patch to the skin. Moreover, it would be possible to have simultaneous interstitial fluid sampling and drug delivery (of insulin, for example) by this arrangement, particularly if more than one set of holes in a microelement were provided (see other such structures, below), or if at least two groups of microelements were provided on a single substrate. A first group (or array) could sample the interstitial fluid, while a second group (or array) could delivery the drug.

Another microelement shape is illustrated in Figure 5, comprising an array 50 of "cubic rectangular" microelements at 52. These microelements 52 have a cup-like shape which has the appearance of a topless, hollow or open cube-like or box-like structure after one of the cube's (box's) side walls have been removed. This can be clearly seen in the perspective view of Figure 6. (It will be understood that the "cube-like structure" 52 does not have identical length, width, and height outer dimensions, and thus is not really a geometric cube. In that respect, the term "box-like" or "box" is more descriptive.)

The individual columns of microelements 52 can be offset on the substrate 54, as seen in Figure 5. As an alternative construction, each of the individual columns of these microelements 52 could be identical, thereby eliminating any offset, if desired. As a further alternative, there could be several columns with various offsets before the microelement pattern repeats, or the offsets could be substantially random so that there is no repetitive pattern.

Figure 6 shows further details of the individual microelement 52, which has a "back wall" 62, a pair of "side walls" 60, a "front edge" at 64 on each of the side walls 60, and a base line 66 along the bottom of the side walls 60.

To penetrate the stratum corneum of skin, the microstructure or "patch" 50 is rubbed back and forth substantially along the direction designated by the letter "C" (which is a preferred, predetermined direction). In this manner, the edges at 64 will cut or lance through the skin cells to a predetermined penetration depth, which will be substantially equivalent to the protrusion distance of the microelements 52.

Figure 7 illustrates a similar array of microelements, designated by the reference numeral 70. Each individual microelement 72 has a similar appearance to the open box-

like microelements 52 of Figures 5 and 6, however, a through-hole 76 has been added within the "cup-like" area of the microelement 72. These holes typically would run completely through the base or substrate 74, although they could instead extend only partially into the substrate to connect to some type of internal channels. In that manner, these holes could become (or connect to) passageways of any shape, diameter, or length.

The microstructure array 70 could be formed into a "patch" that is applied to skin and rubbed in a back and forth manner substantially in the direction "C" indicated on Figure 7 (which is a preferred, predetermined direction). Figure 8 shows further details, in which there are two side walls 80, a back wall 82, two "front" edges 84, a base line 86 for each of the side walls 80, and the through-hole 76 that is proximal to the interior area of the microelement 72. In a similar manner to the previously described microstructure of Figures 3 and 4, the microstructure 70 disclosed on Figures 7 and 8 can be used to simultaneously penetrate the skin surface while delivering some type of active into the epidermis. Such systems can both penetrate the skin's outer layer and deliver to the epidermis in a single operation by a user.

Figure 9 illustrates an array 100 of wedge-shaped microelements 102 mounted onto a base or substrate 104. As in some of the earlier-described embodiments, each column of microelements 102 can be offset from the adjacent column, as illustrated on Figure 9. However, the columns could alternatively be made identical to one another, in which there would be no offset. A further alternative could arrange several columns with various offsets before the microelement pattern repeats, or the offsets could be substantially random so that there is no repetitive pattern.

The wedge-shaped microelement 102 is illustrated in greater detail in the perspective view of Figure 10. The top of the structure is at 114, and there are two elongated side walls 112 and a pair of converging side walls 110 that, at their line of convergence, form a cutting edge 116. There is also a base line 118 at the junction between the side wall 110 and the substrate 104.

The relatively sharp edge 116 is purposefully used to cut or slit (or "lance") the skin in the methodology described in this patent document. The overall wedge shape of the microelement 102 is provided as a more substantial structure than some of the other embodiments described herein. It also is probably easier to manufacture than the

microelements described earlier, in Figures 1-8. In the microelements of the array 100 on Figure 9, it is preferred to apply the array as a "patch" onto skin, and then rub it in a back and forth manner substantially along the line "C" (which is a preferred, predetermined direction). As can be seen from Figure 9, the relatively sharp edges 116 will be used to cut into the skin when the patch 100 is moved in this manner along the line "C".

In essence, the edge 116 will tend to act as a miniature plow against the dead skin cells of the stratum corneum. A more descriptive view of the plowing action is provided in Figure 27, which illustrates one of the "straight" wedge-shaped microelements 102 as it makes a slit or cut in the skin. The skin is depicted at 300, and it can be seen that the sharp edge 116 made up by the two converging faces 110 essentially plows through the top portions of the stratum corneum, starting at the point 302, and thereby parting the skin along the lines at 306. This leaves an inner portion of the skin temporarily exposed at 304.

On Figure 27, the microelement 102 is being moved substantially in the direction of the arrows "C," thereby indicating that the skin is being cut in that direction. Of course, when the microelement 102 is moved in the opposite direction, it will tend to cut the skin in the opposite direction and form a new slit, or enlarge an existing slit.

It will be understood that various depths of the microelements and widths of the microelements can be constructed to increase or decrease the size and penetration depth of the slits made in the skin, and such dimension variations are envisioned by the inventors. Certainly, the exact shapes and sizes can be varied without departing from the principles of the present invention.

Figure 11 shows a similar wedge-shaped microstructure array at 120, which has individual wedge-shaped microelements 122 that have two separate through-holes at 126. The microelements 122 are all mounted on a base or substrate 124. As viewed in Figure 11, the columns of microelements 122 are somewhat different from one another, in that they are offset from one another in adjacent rows. This need not be the case, and alternatively the columns could be identical to one another to eliminate any offset, if desired. Again, alternatively there could be several columns with various offsets before the microelement pattern repeats, or the offsets could be substantially random so that there is no repetitive pattern.

Figure 12 shows further details of the individual microelement 122, in which a top surface 134 and elongated side walls 132 are exhibited, along with converging side walls 130 that come to a sharp edge 136. A base line 138 is also illustrated as the junction between the microelement 122 and the substrate 124. The through-holes 126 are created to penetrate entirely through the microelement 122, and preferably will also penetrate entirely through the base 124, although the holes 126 can become passageways that do not entirely penetrate through the base or substrate, but instead connect to some type of perpendicular runs or passageways, if desired. Since there are two separate holes 126 per microelement 122, it is possible to simultaneously deliver two different actives (one per hole in a single microelement) in a single operation, if desired.

The microelements 122 are designed to perform both a skin penetration function and a delivery procedure in a single step. In this particular structure, it can almost be guaranteed that there will be a lack of build-up of dead skin and other foreign matter within the delivery holes or passageways 126. Even if some of this foreign matter or dead skin cells accumulates in these passageways 126, a capillary action may result and accomplish delivery of at least one active or drug through the passageways 126 and into at least the epidermal layer of the skin.

Figure 13 illustrates a microstructure array designated by the reference numeral 140 that contains a large number of individual wedge-shaped microelements 142 that are mounted to a base or substrate 144. These wedge-shaped microelements 142 contain a through-slot 146, through which at least one active or drug can be delivered through the outer skin surface just after the stratum corneum has been penetrated. In a similar manner to the structures of Figure 11, the microelement array or patch 140 will preferably be placed on the skin surface and rubbed in a back and forth manner substantially along the direction "C" (which is a preferred, predetermined direction) to penetrate or cut skin cells of the stratum corneum.

Figure 14 shows greater details of an individual microelement 142, showing a top surface 154, side walls 152, converging side walls 150 that come to a relatively sharp edge 156, and a base line 158 where the microelement 142 adjoins the base or substrate 144.

The through-slot 146 can provide a larger cross-sectional area for delivery of at least one active or drug to the skin surface, as compared to the microelement 122 of Figure 12. Of course, the actual dimensions of the microelement 142 could be either larger or smaller than similar microelements 122 illustrated on Figure 12. Both sets of microelements 122 and 142 are relatively simple to construct, although the ones with the through-slot 146 may be somewhat easier to construct as compared to constructing multiple smaller through-holes 126.

The patch or array 140 can be used for a combinational step of skin penetration and delivery of at least one active, in a similar fashion to that described in some of the earlier embodiments. Other similar shapes of wedge-shaped structures could easily be constructed without departing from the principles of the present invention.

Figure 15 discloses an array or patch 160 of triangular-shaped wedge microelements 162, mounted on a base or substrate 164. As seen in Figure 16, each of the microelements 162 consists of an elongated triangular shape, having a pair of triangular side walls 170, a pair of sloped elongated side walls 172, a top edge 174, and a pair of base lines 178. The junction between the triangular end walls 170 and the rectangular but sloped side walls 172 is designated at the reference numeral 176. The peak of the triangle is illustrated at 174, which is only one point along the top edge 174 of the microelement 162.

These triangular-shaped wedges can be useful in a skin penetration procedure, and preferably will be placed on skin in the form of a patch and then rubbed back and forth over the skin substantially in the direction "C" (which is a preferred, predetermined direction). The individual columns of microelements can be offset from one another in adjacent columns, as seen in Figure 15. Alternatively, the columns could be identical to one another, without any offset. Another alternative could arrange several columns with various offsets before the microelement pattern repeats, or the offsets could be substantially random so that there is no repetitive pattern.

Figure 17 discloses a similar microelement array 180, which has triangular-shaped wedges as individual microelements 182 that are placed or are formed upon a base or substrate 184. In the "patch" 180, there are multiple through-holes 186 and channels 188 for placing at least one active through the stratum corneum.

Figure 18 shows the channels 188 and holes 186 in a magnified view, in which the holes 186 would typically be designed to penetrate entirely through the substrate 184; however, such holes 186 could only partially penetrate the base if they connect to some other type of passageway within the base structure itself.

The triangular shape of the microelement 182 is seen on Figure 18 along the side wall 190, which connects to sloped, rectangular side walls 192 along edges 196. A top edge 194 exists between the two triangular side walls 190, and a base line 198 marks the line between the microelement 182 and the substrate 184.

On Figure 18, there are three separate channels 188 in the surface of the elongated side wall 192. Of course, fewer channels could be utilized, if desired, or even more numerous channels could be used. These channels 188 lend themselves well for capillary action to allow at least one active to flow through the holes 186 and along the channels 188 into the stratum corneum, even if the areas between the microelements 182 become substantially full of dead skin cells and other foreign substances.

The triangular wedge structures of both Figures 16 and 18 are basically designed to penetrate the stratum corneum layer of skin. This is accomplished by moving the microelement patches 160 or 180 in a back and forth manner substantially in the direction "C" as shown on Figures 15 and 17. Of course, if the microelement patches were to be moved in a different direction, particularly one that was perpendicular to the line "C" (which is a preferred, predetermined direction), then it is quite likely that the skin would not be cut and penetrated (at least not to the extent as compared to when the patch is used in the intended "C" direction). This has much usefulness, however, that concept is not part of the present invention. Instead, that type of methodology is disclosed in a companion patent application, filed on September 14, 2001 under Serial Number 09/952,403, which is also assigned to The Procter & Gamble Company, and having the title "Microstructures for Treating and Conditioning Skin."

Another refinement of the triangular-shaped wedge is illustrated on Figures 19 and 20. On Figure 19, a microstructure array or patch 200 is illustrated as containing multiple wedge-shaped microelements 202 that are placed upon, or are formed thereon, a base or substrate 204. As seen in Figure 20, each of the microelements 202 is comprised of three separate triangular-shaped wedges, each having a space therebetween at 206.

On Figure 20, it can be seen that the three sections of the triangular-shaped wedge 202 includes a triangular-shaped side wall 210, a pair of rectangular, sloped side walls 212, a top edge 214, and a base line at 216 where the microelement 202 joins the substrate 204. Each of the three wedge shapes is separated by a space 206, in which a center triangular wedge shape is surrounded on both sides by a second, outer similar wedge shape, and spaced apart from each of these outer wedge shapes by the spacing area 206.

The three separate wedge shape of microelement 202 (which are separated by the spaces 206) provide more individual cutting edges 214. Each peak of a triangular end wall 210 represents a new cutting or "plowing" point when the patch 200 is moved substantially along the line "C".

The preferred use of the array or patch 200 is to apply the patch directly to the skin, and then rub the patch in a back and forth manner along the skin surface substantially in the direction "C" as seen on Figure 19 (which is a preferred, predetermined direction). This particular design penetrates the skin outer layers quite well, but is not designed to also apply an active at the same time. Of course, through-holes and channels could be added to this structure, if desired, although that type of structure would probably be easier to construct when using the shape disclosed in Figure 18 for the microelement 182.

It will be understood that a microelement patch could be composed of any one shape of microelements, or could be comprised of several different shapes on a single substrate or patch structure, without departing from the principles of the present invention. Moreover, it will be understood that the microelements disclosed herein could be of all the same height, or of different heights on the same substrate or patch, without departing from the principles of the present invention. Finally, it will be understood that minor modifications to the shapes disclosed in the drawings are contemplated by the inventors, and would still fall within the principles of the present invention.

It will also be understood that the microelement arrays or patches that contain through-holes or through-slots need not have such through-holes or through-slots for each and every one of the individual microelements that make up the array. In other words, the passageways that flow through the microelements (or adjacent thereto) could be

constructed on only one-half of the microelements, if desired, while still achieving most of the results that would otherwise be achieved if such through-holes or through-slots were found at each of the microelements. Certainly, the holes or slots could be varied in size or diameter to either reduce or increase the amount of fluidic material that flows therethrough. All of these variations are contemplated by the inventors, and would fall within the principles of the present invention.

In general, the microelements of the present invention described above are longer than those used only for exfoliation, and the lengths of the microelements would typically be in the range of 50-1000 microns. This will allow the microelements to penetrate the stratum corneum. As noted above, on Figures 1, 3, and 21, the direction of sliding the patch is not important; however, on Figures 5, 7, 9, 11, 13, 15, 17, and 19, the direction of sliding is more important, and should be substantially in the direction as depicted by the arrow "C." This will allow the microelements to cut the skin, and to penetrate the skin to a depth that will pierce the stratum corneum to a certain extent. This will allow an active or other type of fluidic material or fluidic compound (such as a liquid or a cream) to penetrate much more easily through the stratum corneum.

Figure 21 illustrates a "coiled appendage" of a sort, in which multiple curved wedge-shaped microelements at 222 are placed on a substrate 224 to form an array or patch generally designated by the reference numeral 220. Figure 22 illustrates one of these arcuate microelements 222 in greater detail. The microelement 222 includes two wedge-shaped points that are made up of relatively flat surfaces 230 that converge at an edge 236. The two wedge-shaped "cutting surfaces" at the edges 236 are joined by a curved body that has side walls 232, a top surface 234, and a base "line" at 238 that is curved or arcuate in shape.

The array or patch 220 is used by placing the patch on the surface of skin, and then rotating the patch substantially along the arc designated at the letter "C." This will tend to slit or otherwise cut the skin along the relatively sharp edges 236 in either direction of the curved microelements 222.

The curved microelements 222 on the array/patch 220 can be used in two methodologies: (1) the skin is first cut, the patch 220 removed, and then a fluidic compound (e.g., a liquid material or cream) is applied to the skin; (2) the fluidic

compound is applied first to the skin, then the array/patch 220 is pressed down on the same area of the skin and rotated to create the openings, thereby allowing the fluidic compound to penetrate more easily through the stratum corneum.

A similar arcuate or curved wedge structure is illustrated in Figure 23, in which the individual microelements at 242 are placed upon a substrate 244 to make up an array or patch 240. These curved wedges also may be referred to as "coiled" structures. One of the microelements 242 is illustrated in greater detail in Figure 24, and it can be seen that through-holes 246 are placed through the top surface 254 of the microelement 242. This will allow a fluidic compound to pass through the holes 246 and into the skin after the stratum corneum has been slit or otherwise pierced by the arcuate microelements 242. Each curved microelement 242 exhibits a pair of sharp edges at 256 that are made up by relatively flat sides 250 that converge along the line 256. The curved structure has side walls 252, a top surface 254, and a base "line" or arc at 258 where the microelement 242 joins the substrate 244.

In the structures of Figures 23 and 24, the patch 240 would typically be placed upon the skin surface and then rotated substantially in the direction designated by the curve "C." The fluidic compound that is to penetrate through the stratum corneum is already contained within some type of reservoir or chamber (or perhaps a non-woven impregnated material) that will then seep through the holes 246, including by capillary action.

An alternative structure is illustrated in Figure 25, in which the curved microelements 262 exhibit through-slots at 266 that are also arcuate in shape. The curved microelements 262 are placed upon a substrate 264, and the overall structure makes up an array or patch 260. Figure 26 shows the individual microelement 262 in greater detail, and illustrates the sharp edges at two of the ends of the curved microelement at 276, which are made up of converging side walls 270. A curved side wall 272 is illustrated, along with a top surface 274 and a base "line" or arc at 278 where the microelement 262 joins the substrate 264. The through-slot 266 is easily visible in Figure 26.

The arcuate microelement 262 is used in a similar manner to that illustrated in Figure 24, in which the array/patch 260 is placed upon skin and rotated substantially

along the arc "C," and then a fluidic compound is allowed to pass through the slot 266 through the stratum corneum, as desired.

Figure 28 illustrates the wedge-shaped microelement 102 from its "sharp" end in an elevational view. The two converging sides 110 are seen to form a relatively sharp edge at 116, which travels vertically from the top of the substrate/base 104 to the top surface 114 of the microelement 102. The angle "A" between the substrate top surface at 104 and the side wall 112 is clearly visible. On Figure 28, this angle "A" is approximately 90°, and therefore forms a perpendicular angle.

Figure 29 shows an alternative shape for a wedge-shaped microelement designated by the reference numeral 402. This wedge-shaped microelement has a similar appearance from above to that of the wedge-shaped microelement 102, except that its elongated side walls are not formed by a perpendicular angle to the substrate.

On Figure 29, the substrate 404 is joined to the outer wall that is elongated along the side of the microelement (i.e., the wall 412) by an angle "A" that is greater than 90°. Its complimentary angle is illustrated at "B." Angle B is between 45° and 60° in Figure 29, but of course could be any angle that will successfully operate to penetrate the skin.

The front walls that converge are illustrated at 410, and converge along the relatively sharp edge at 416. This non-perpendicular wall shape of a microelement 402 may have some advantages with regard to manufacturing and with regard to overall strength of the structure.

Figure 30 is a side elevational view in partial cross-section of a microstructure that contains an array of different shaped microelements and a corresponding substrate, designated at the reference numeral 460, as well as an underlying reservoir structure designated by the reference numeral 470. On Figure 30, the array of microelements 460 is illustrated as having a set of pyramidal microelements 32 having grooves or channels 38 along the sides of the pyramid shapes, and a set of wedge-shaped microelements 122 having through-holes 126. The base or substrate is designated at the reference numeral 462.

On Figure 30, the through-holes actually travel all the way through both the microelements and the substrate 462 to form passageways, and these passageways are depicted in two groups. The first group is a combination of the grooves or channels 38 in

the pyramidal microelements 32 that are connected to the through-holes 464, to form a common set of passageways that extend from the bottom surface of the base or substrate 462 through the top surface of this substrate 462 and are in communication with the channels or grooves 38. The second set of passageways comprises a set of through-holes 466 that are in communication with the microelement through-holes 126 of the wedge-shaped microelements 122. These through-holes 126 and 466 must be in registration with one another to form complete passageways from the top of the microelement 122 to the bottom of the substrate of 462. Naturally, there could be some horizontal runs that connect similar passageways, if desired.

The bottom portion 470 depicted in Figure 30 includes a reservoir structure that has a bottom wall at 472 and a reservoir area or volume at 476 that is bounded by the side walls of the reservoir at 474. Multiple such compartments or chambers can be constructed to house multiple actives. The upper portion of this reservoir structure 470 would typically be planar, as depicted at the reference numeral 478, and would make contact against the bottom surface at 468 of the microstructure/substrate apparatus at 460. It is important that the reservoir 476 be in communication hydraulically or pneumatically with the passageways 464 and 466, thereby allowing a fluidic drug or other active to reside within the reservoir confines at 476 until used, and then for the fluidic drug or active to be directed through the passageways 464 and 466 to the upper surface of the microelements 32 and 122.

Figure 31 illustrates an array of wedge-shaped microelements 102 on a substrate 104 that makes up a microstructure apparatus designated by the reference numeral 100. Microstructure apparatus 100 comprises a top layer that is laminated to a non-woven backing 502, which is preferably thin enough so as to be substantially flexible. This overall structure is generally designated by the reference numeral 500 on Figure 31.

The top layer 100 that contains the multiple microelements 102 can have as a substrate and microelement material some type of moldable plastic, such as nylon, or a polycarbide material, or PMMA, for example (and these materials may be used with any microelement shape). The bottom or backing material 502 preferably is a substantially flexible material that exhibits a soft texture. Typically a non-woven material gives an impression of cloth, and thus can provide the desired soft texture.

The non-woven backing material 502 can be laminated with the microelement layer 100 by use of a chemical glue or a heat-activated adhesive, for example. On Figure 31, the non-woven backing is somewhat larger in length and width than the microelement layer 100, and thus can be seen along the edges.

Figure 32 illustrates a similar laminated structure, however, the microelements 102 are formed as strips 512, in which there are several such strips that contain rows of the microelements. The non-woven backing material can be seen both along the top and bottom edges, and also between the strips at 514 on Figure 32. The overall structure is generally designated by the reference numeral 510.

In Figure 33, the microelements 102 are visible at the top, as residing above the substrate 104. The bottom portion of the substrate is permanently affixed to the non-woven backing material 502, thus leading to the overall structure at 500.

As discussed above, the fixing of the non-woven backing material 502 to the substrate 104 can be by some type of adhesive used in lamination, or perhaps using a sonic bonding process. Alternatively, a co-extruded material could be used.

One major advantage to using a non-woven backing material as depicted in Figures 31-33 is that this non-woven material 502 (or 514 on Figure 32) can be impregnated with at least one active, and thereby effectively become a "reservoir" without creating an actual chamber having an open volumetric space. This not only saves a manufacturing procedure step by not requiring a true open chamber to be constructed, but also allows the overall structure of the "patch" shown in the earlier figures to be made of a substantially flexible material that is much less likely to exhibit breakage problems.

It will be understood that various shapes of microelements can be used with the non-woven backing material, and various shapes of substrates can be laminated or otherwise affixed to the non-woven backing material. It will also be understood that the backing material may or may not be impregnated, all without departing from the principles of the present invention. Finally, it will also be understood that other suitable materials besides non-woven materials could be used for the backing at 502 and 514 on Figures 31 and 32, all without departing from the principles of the present invention.

Figure 34 illustrates a completely different approach in microstructures for penetrating skin as compared to the above-described microstructures. A rotatable

structure, generally designated by the reference numeral 600, is covered with a plurality of microelements 602 that protrude or extend from a cylindrical substrate 604 (i.e., affixed on a curved substrate). As illustrated on Figure 35, each of the microelements 602 has a wedge-shaped pair of edges at 616, which are formed by side walls 610 that meet at the edge 616. The side walls 610 are separated from the two longitudinal distal ends or edges (at 616) by another side wall 612 which appears on both sides of the microelement 602. The side walls 612 and end walls 610 are bounded by an upper surface 614, which includes a through-slot generally designated by the reference numeral 606. A fluidic material that is stored inside the cylindrical-shaped rotatable structure 600 can flow out through the slot 606, thereby having the capability of being dispensed into skin.

The microelements 602 are very similar in shape to those described on Figures 13 and 14 above, at the reference numeral 142. The microelements 602 are designed to penetrate into the skin and through the stratum corneum, thereby enabling the fluid material being dispensed through the slot 606 to penetrate into the skin.

A quite unique structure is thereby disclosed, in which the rotatable structure 600 has an axle member at 608, which can be attached to some type of roller-structure, thereby enabling the cylindrical shape of the rotatable structure 600 to rotate in both directions indicated by the arrow "C." Ideally, the cylindrical structure 600 will be placed upon skin and then translationally moved such that the cylinder rotates while moving along the surface of the skin, thereby enabling the individual microelements 602 to cut into the skin and penetrate the stratum corneum while the structure 600 is being rotated.

A variation of the rotatable structure 600 is illustrated on Figure 36, in which microelements generally designated by the reference numeral 622 have a different shape than those microelements 602 found on Figures 34 and 35. The overall rotatable structure is generally designated by the reference numeral 620 on Figure 36, and exhibits a cylindrical shape that is made up of a substrate 624 that has a plurality of individual microelements 622 protruding or extending therefrom. As the rotatable structure 620 is rotated and pressed against skin, the sharp edges of the microelements 622 will penetrate the skin, preferably through the stratum corneum, as the cylindrical structure 620 is rotated in either direction indicated by the arrow "C."

An enlarged view of a single one of the microelements 622 is provided on Figure 37, in which side walls 630 come together at substantially sharp edges 636. These sharp edges are such that they can penetrate the stratum corneum of skin when pressed down against the skin while the cylindrical structure 620 is rotated. The top edges of the side walls 630 are bounded by a top surface 634.

Both Figures 36 and 37 illustrate a plurality of openings or through-holes 626, which are placed around the microelements 622. If a fluidic material (e.g., drug) is disposed within the cylindrical structure 620, then that fluidic material can pass through the openings 626 and onto the skin as the structure 620 is rotated in the direction C.

If the rotatable structure 600 or rotatable structure 620 is rotated quickly, then due to centrifugal force, the fluidic material will be forced through the openings (either the through-slots 606 or the through-holes 626). However, a more positive pressure can be created by other structures, which will be discussed below. These alternative pressure sources also can be activated by the rolling motion.

It will be understood that the microelements and substrate combination can be formed as a sheet that is sufficiently flexible to be wrapped around in the shape of a cylinder. In such a circumstance, the sheet structure could be formed from an embossing procedure, or perhaps from a molding procedure. If the embossing procedure is utilized as the fabrication methodology, then a continuous embossing operation would likely be chosen by a manufacturer. As an alternative, the cylindrical shape could be formed directly by a molding process.

It will also be understood that the actual placement of the microelements on the outer surface of the cylinder can be essentially of any pattern chosen by a designer, in which the microelements could be formed in straight lines, or in a staggered configuration, or perhaps in a more random-like pattern. Essentially any set of distances between microelements and patterns in their layout on the cylindrical surface are contemplated by the inventors, and would not depart from the principles of the present invention.

Figure 38 illustrates another alternative embodiment of a cylindrical-shaped rotatable structure that contains a plurality of microelements thereon. The overall cylindrical structure is generally designated by the reference numeral 640, which contains

a plurality of microelements 642 that are placed upon or protrude from a substrate 644. A plurality of openings or through-holes are indicated at 646, which would allow a fluidic material stored within the rotatable structure 640 to pass therethrough and onto the surface of skin. The microelements 642 are shaped to penetrate skin at least through the stratum corneum layer, thereby allowing the fluidic material to penetrate into the skin as the cylindrical structure 640 is rolled upon the skin surface.

In Figure 38, the individual microelements are not symmetrical in shape, as opposed to those microelements 602 and 622 that were disclosed in Figures 34-37. As can be seen in Figure 39, the microelement 642 is shaped like a right triangle in this side view, which exhibits a side wall 650 that comes to a point at a distal end 656. When the cylindrical structure 640 is rotated in the direction of the arrow "C," it can be seen in Figure 39 that the side of the triangle with the distal point at 656 will much more readily penetrate into the skin, which is designated at the reference numeral 658. Of course, if the hypotenuse 652 (see Figure 40) of the triangle-shaped microelement 642 was sharp enough between the side walls 650, then these microelements may also penetrate the skin while being rolled in the opposite direction from the arrow C; however, that is not the main intent of this embodiment.

Alternative microelement shapes are disclosed in Figures 40-42 that can be used with the cylindrical structure 640. On Figure 40, the microelement 642 is illustrated as exhibiting two side walls 650 which have a common edge therebetween at 652. A triangular end wall is formed at 654, which can also be seen on Figure 38. The peak of this triangular end wall 654 is at the distal end or point mentioned above, at reference numeral 656. It is this point that is to make the main penetration into the skin.

In Figure 40, a side view D-D of the microelement 642 is depicted as having a right angle which is bounded by a horizontal line on this figure, and a vertical line which is designated by the reference numeral 654. Reference numeral 654 in actuality is the triangular end wall that was described above. The side wall 650 is illustrated as having a peak point at 656, which runs down a hypotenuse 652. The right angle between the horizontal line and the vertical end wall 654 form an angle referred to as "Z" on Figure 40.

There are two elevational views on Figure 40; the first view is designated A-A which illustrates the end wall 654 as being triangular in shape, having two side walls 650 which come to a point at the distal end or peak at 656. It will be understood that the triangular shape in view A-A can be an equilateral triangle, or it could be an isosceles triangle which would have two equal sides made up by the line segments 650 on view A-A. Of course, a non-isosceles could be provided if desired. The other elevation view is B-B, which is from the opposite end of the microelement 642. View B-B shows the side walls 650 which are joined at a relatively sharp edge 652, which all intersect at the top peak or point at 656.

Figure 41 illustrates an alternative embodiment for a microelement to replace or be used in conjunction with the microelements 642 that appear on Figures 38-40. The alternative microelement of Figure 41 is generally designated by the reference numeral 668. As can be seen on Figure 41, microelement 668 has a different angle Z that can be viewed from a side view E-E, which shows the side wall 660 as having a triangular shape, although the angle Z is an obtuse angle rather than a right angle. The end wall of microelement 668 is designated at the reference numeral 664, which would still have triangular shape and come to a top point or peak at a distal end or point 666. The hypotenuse of the triangle seen from the side view E-E is designated at the reference numeral 662. In the other view of Figure 41, both side walls 660 are seen as meeting at an edge 662 (which is the hypotenuse of the triangle seen in the other view). It can be seen that the top or distal point 666 will form the primary cutting surface when the microelement 668 is moved in the direction C by rotation of the cylindrical structure, similar to that viewed in Figure 38.

Figure 42 is another alternative embodiment of the microelement 642, in which the alternative microelement, generally designated by the reference numeral 678, exhibits an acute angle at Z, as seen in the side view G-G showing the side wall 670. In this view G-G, the acute angle Z is bounded by a horizontal line and an end wall 674, which comes to a top point or peak at a distal end or point 676. The hypotenuse of this triangular shape is at the reference numeral 672.

An end view F-F is also provided on Figure 42, in which the end wall 674 is illustrated as having a triangular shape, made by the side walls 670, which meet at the top

peak or point 676. It will be understood that the triangular shape of the end wall 674 can be equilateral, isosceles, or non-symmetric overall, as desired by the microstructure designer.

The top view of Figure 42 illustrates the microelement 678 as having two side walls 670, an end wall 674, all of which meet at the top point or peak 676. The two side walls 670 meet along an edge line at 672, which forms the hypotenuse in the view G-G. As can be seen in Figure 42, the shape of the microelement 678 will allow its end wall surface 674 in conjunction with the top peak or point 676 to readily penetrate skin when the microelement 678 is moved in the direction C, typically by rotation of a cylindrical structure similar to that of 640 in Figure 38.

The next few figures starting with Figure 43 illustrate various alternative embodiments for use with the rotatable structure 600 that contains a large plurality of microelements 602. It will be understood that any appropriately-shaped microelement could be used for virtually any of these alternative embodiments without departing from the principles of the present invention. Keeping in mind that the main purpose is to penetrate skin, all of the microstructures disclosed in the next few figures can penetrate the stratum corneum and deliver a drug or other fluidic compound through the stratum corneum and into the skin.

Referring now to Figure 43, a hand-held roller-structure generally designated by the reference numeral 700 is depicted, which has a chassis or body 702, three axles at 608, and three cylindrical structures 600 that contain the microelements. When this roller-structure 700 is pressed against skin 704, and moved in either direction of arrows "C," then the microelements will penetrate through the top layers of the skin (i.e., at least through the stratum corneum), thereby allowing delivery of a drug or other fluid compound into the skin. It will be understood that this embodiment 700 could alternatively comprise a single cylindrical roller 600, or a much larger number of such rollers, as desired by the designer of the microstructure system. Moreover, if multiple cylindrical structures are used in the overall device 700, then the pattern of microelements for the different rollers could be the same, or could be different if desired. The use of the word "pattern" implies either the same shaped microelements in different configurations as to their positions on the substrates of one of the cylindrical rollers, or different shaped

microelements on different rollers, in which a first microelement shape is found on a first roller 600 and a second microelement shape is found on a second roller 600, or some combination of shapes on a single roller.

Referring now to Figure 44, a single roller 600 is illustrated, in which this single roller is a rotatable structure that contains a large number of microelements. The roller 600 is attached to an arm 714, that is further attached to an extending member 712 that can be held by a person's hand. The overall structure is generally designated by the reference numeral 710, which contains the member 712, the arm 714, and the cylindrical rotatable roller-structure 600. When this structure 710 is held such that the cylindrical rotatable roller-structure 600 is placed upon skin 718 and then moved in either direction designated by the arrows "C," then the individual microelements will penetrate the skin (preferably through the stratum corneum layer) so as to allow delivery of a drug or other fluidic compound into the skin. As noted above in reference to Figure 43, the microelements on the roller 600 can be of the same type (i.e., size and shape) and can be laid out in a symmetrical pattern such as straight lines, or alternatively can have a staggered configuration, or with another alternative in mind, the microelements can be of different sizes and shapes, if as desired by the designer of the microstructure. Another alternative embodiment is illustrated in Figure 45, in which an overall hand-held roller-structure generally designated by the reference numeral 720 provides a cylindrical roller, which is designated by the reference numeral 601. A main body or chassis 722 is contacted by a person's hand, and this body 722 contains a reservoir at 724 which contains a fluidic compound 726. The fluidic compound 726 is dispensed by the person pressing down on a top button 728, which produces pressure inside the reservoir (or chamber) 724. When this occurs, the fluid 726 will be dispensed through a pathway to an outlet port 728 that is in proximity to the surface of the skin at 730.

The cylindrical surface of roller 600 can be made disposable for one-time use applications. It will be understood that the microstructure cylindrical surface can be made disposable for all of the embodiments disclosed in this patent document, including the "chassis" embodiments such as illustrated in Figure 43.

It will also be understood that there is some benefit in destroying the functionality of the microelements after they have been used, particularly for one-time usage

applications (i.e., with disposable rollers or disposable sliding members, etc.). The destruction process can be achieved using a built-in device if desired, or it can be achieved using an independent, separate microelement destructive apparatus, that crushes or melts the sharp edges, for example.

The body or chassis 722 also contains an axle 608 that holds the roller 601 in place. When the overall roller-structure 720 is moved in the direction of the arrow "C," then the fluid that is dispensed through the outlet port 728 forms a thin layer on top of the skin surface, as seen at 732 on Figure 45. The rotatable roller 601 will pass over this layer of fluid 732 and, as the microelements cut into the skin through the stratum corneum layer, the fluid layer 732 will be forced down and through these openings in the skin to become a "layer" of fluid beneath the top layer of the skin, at 734 on Figure 45. As in the other embodiments disclosed in this patent document, the exact size and shape of the microelements on the rotatable roller 601 can be of many different sizes and shapes, while serving the purposes of cutting through the stratum corneum layer and allowing the fluid to be passed through the stratum corneum and into the skin, all without departing from the principles of the present invention.

In this roller-structure embodiment 720, the microelements formed on the cylindrical surface of the roller 601 would typically have no openings, and would comprise microelements that form protrusions only. It will be understood that the pressure at the outlet port 728 can be controlled by the aperture size and/or the shape of the fluid pathway, thereby controlling the rate of fluid dispensing.

Another alternative embodiment of the present invention is illustrated in Figure 46, in which an overall roller-structure 740 comprises a main body or chassis 742, which contains a different type of fluid chamber therewithin, and also comprises another microelement cylindrical roller. As the main body 742 is held by a person's hand, the entire roller-structure 740 can be pushed in the direction of the arrow "C," which will cause the cylindrical rotatable roller 601 to rotate about an axle 608. This rotation causes a worm gear 760 to turn, through a gear box 603 that can be used to control the ratio of turning between the worm gear 760 and the cylindrical roller 601.

Worm gear 760 interacts with a lead screw 762, which interacts with a traveling nut 764 that is located within a reservoir or chamber 744. When the worm gear 760 and

lead screw 762 turn in the correct direction, the traveling nut 764 will move toward the right as seen on Figure 46, thereby squeezing a fluidic material 746 out of the reservoir, and through an outlet fluid path to an outlet port 748, which is in close proximity to the top surface of skin 750.

It will be understood that a small one-way clutch could be included within the gear box 603 to prevent the traveling nut 764 from moving along its translational axis if the roller-structure 740 is moved in the direction opposite that shown by the arrow C. This is an option, and would not be entirely necessary if cost considerations were of paramount importance.

When the fluid is dispensed through the outlet port 748, it forms a thin layer at 752 on top of the skin surface 750. When the cylindrical roller 601 comes along and presses against the skin and this fluid layer 752, it both cuts through the stratum corneum layer and forces the fluidic material in layer 752 through the newly formed openings in the stratum corneum, thereby placing the fluid beneath the skin and forming a "layer" as seen at 754 on Figure 46.

It will be understood that the microelements formed on the surface of the cylindrical roller 601 would typically not have through-holes or other types of openings, and instead would comprise protrusions only, since no fluid need be dispensed from the inner workings of the cylindrical roller 601. Furthermore, the microelements formed on the cylindrical surface of roller 601 can be of virtually any size and/or shape or pattern, as desired by the designer, to meet a specific application, without departing from the principles of the present invention.

Another alternative embodiment is illustrated on Figure 47, in which a fluidic chamber or reservoir is depicted as being separated by a traveling nut 764, in which fluid material to the right of the traveling nut 764 (in this view) would be located within the volume 746, and the remaining portion of the chamber would be located to the left of the traveling nut, in the volume 744. The traveling nut 764 can be moved by rotation of a lead screw 762, which when rotated in the direction depicted by the arrow "R," would cause the traveling nut to move toward the right, and any fluid within the chamber 746 would be dispensed through an outlet port and further into another volume or space that provides fluid through multiple openings at 749. This structure could be utilized in the

moveable apparatus illustrated in Figure 46, and the multiple outlet ports 749 would allow for a relatively wide swath of fluidic compound to be dispensed upon the surface of skin. Bearing that in mind, a cylindrical roller-structure containing microelements for cutting through the stratum corneum layer would likely be disposed such that the longitudinal axis of the roller-structure would be parallel to the longitudinal axis of the lead screw 762.

The next three figures, Figures 48-50, illustrate yet further alternative embodiments in which a cylindrical and rotatable apparatus is utilized to dispense a fluidic compound through multiple openings in multiple microstructures. Referring now to Figure 48, a cylindrical rotatable apparatus 770 is illustrated, which includes an axle 608, a cylindrical substrate 604, and a plurality of microelements 602, similar to the structure 600 that was first illustrated in Figure 34. The overall apparatus 770 also includes a dosing paddle 774 that rotates about the longitudinal axis of the axle 608, when the cylindrical structure 600 is rotated in the direction of arrow "C." A fixed paddle 772 is used as the beginning stop and end stop of the moving paddle 774. A ratchet 776 and paw 778 are used so that the dosing paddle 774 will move only when the structure 770 is rotated in the direction C, and not when the structure 770 is rotated in the opposite direction.

When the dosing paddle 774 moves in an angular manner, it will tend to squeeze fluidic material within the overall cylindrical roller 600 and create pressure, thereby squeezing the fluidic material out through openings 606 in the microelements 602. It will be understood that virtually any size or shape microelements could be useful in this type of embodiment, as desired by the designer of the microstructure system.

A gear system could be added to the overall structure 770 to prolong the dosing if that is desired. With or without a gear system, the overall structure 770 could be manufactured such that the dosing paddle 774 makes a complete revolution from its beginning stop to its end stop position rather quickly, upon rotation of the structure in the direction of arrow C.

In Figures 49 and 50, another alternative embodiment for a dispensing structure, generally designated by the reference numeral 780, is illustrated. The assembly 780 comprises an outer drum 781, an inner drum 782, a wiper or rotatable paddle 783, a

planetary plate 784, a planetary gear 785, and at least one support 786. The support 786 (or pair of supports) cooperates with a handle that is not illustrated on these figures.

The outer drum 782 incorporates a plurality of microelements 787 which contain dispensing openings or through-holes 788. A central shaft 789 provides bearing support for the ends of the outer drum 781, and the shaft 789 is in turn supported by the support 786 (or a pair of supports). A bearing aperture 761 of the outer drum 781 extends inwardly through a boss 763, which in turn incorporates gear teeth 765 about its outer diameter.

The central shaft 789 also provides bearing support for the inner drum 782. Inner drum 782 includes an inner drum flange 767 which has an inner diameter surface that is provided with gear teeth 769 which have the same size and pitch as the gear teeth 765. The shaft 789 provides bearing support for the planetary plate 784 between the boss 763 and the outer drum 781, and the closed end of inner drum 782.

The planetary gear 785 incorporates a spindle 751 that is rotatably and slideably mounted within a slot 753 in the planetary plate 784. Slot 753 is so constructed that one end is further from the outer diameter of the planetary plate 784 than its other end. As the planetary gear 785 is driven up the slot 753, it is placed into operating cooperation with the gear teeth 765 and 769. If the assembly 780 is rotated in the opposite direction, the planetary gear 785 is driven down the slot 753 and out of mechanical cooperation with the gear teeth 769. The result of this construction is that the planetary gear 785 will function as an overrunning clutch, providing one-way rotation to the inner drum 782.

The inner drum 782 includes an internal dam 755 that moves slowly away from the wiper 783 which is rigidly affixed to the non-rotating shaft 789. The inner drum 782 is also provided with slots or holes 757 which protrude therethrough, in which these slots or openings are located transversely across the drum 782 on the opposite side of the dam 755 from the wiper 783. The internal dam 755 extends inwardly to slideably touch the shaft 789. In this manner, an inner reservoir at reference numeral 759 is formed within the inner drum 782, and this inner reservoir slowly decreases in volume as the assembly 780 is operated. It should be noted that the rate of decrease of the volume of inner reservoir 759 is predetermined by the gear ratios of the planetary gear set, and also that the inner drum 782 rotates at a substantially slower rate than the outer drum 781.

If a fluidic material is placed within the reservoir 759, when the roller unit 780 is rotated or rolled in the direction C along a surface (such as skin), the liquid is slowly forced out through the slots or openings 757 into an outer reservoir at 741. The liquid will then disperse throughout this reservoir 741 to substantially uniformly supply fluid to the plurality of dispensing openings or holes 788 with a metered flow of the fluid.

As the outer drum 781 rotates clockwise (as viewed in Figure 49), the planetary gear 785 is driven counterclockwise (in this same view) by virtue of the gear teeth 765 that are incorporated into the outer diameter of the boss 763. The planetary gear 785 is also driven to the "top" of the slot 753, where it is forced into cooperation with the gear teeth 769 of the inner drum 782. The inner drum 782 will rotate counterclockwise (in this view) at a reduced rate when this occurs.

If the outer drum 781 is rotated in a counterclockwise direction (as viewed in Figure 49), the planetary gear 785 will be driven in a clockwise direction (in this view) which causes it to translate to the "lower" end of the slot 753. When this occurs, the inner drum 782 will become disengaged and will not reverse rotate. Both ends, or only one end, of the roller assembly 780 can be provided with one or more planetary gear sets.

Figures 51 and 52 illustrate another embodiment of a cylindrical-rolling microstructure that is generally designated by the reference numeral 790. The rotatable structure 790 includes as its skin penetrating structure a cylindrical microstructure 600 that contains a plurality of microelements 622, similar to those disclosed in Figures 36 and 37. This cylindrical microstructure rotates on an axle 608, and, for reasons described below, has a single preferred direction of rotation as illustrated by the arrow "C."

On the outer ends of the overall apparatus 790 are two sets of skin-engaging screw threads 792 and 794. (These threads comprise a "skin engagement area.") As best seen in Figure 52, the shape of the individual threads will have an effect on the skin surface, and the purpose is to stretch the skin between these outer ends containing the threads 792 and 794. For example, in the threads 792, the general shape of individual threads is indicated at 793. When the apparatus 790 is rolled or rotated in the direction C, the shape of the thread 793 will tend to pull the skin to the left as viewed on Figure 52. In a similar manner, the general shape of the threads 794 is shown as the individual threads 795,

which will tend to pull the skin to the right as viewed on Figure 52 when the apparatus 790 is rolled in the direction C.

The result of employing the sets of threads 792 and 794 on the ends of the cylindrical apparatus 790 is that the skin will be stretched taut in the area illustrated at 796 on Figure 52, whereas the skin at the areas 798 on Figure 52 will tend to be somewhat bunched up. In this manner, the threads will "catch" the skin (assuming the threads are deep enough) and maintain contact with the skin without allowing much in the way of slippage of the skin. This can enhance penetration of the skin by the microelements by tightening the skin in the direction of dosing using a fluidic compound, such as a drug.

It will be understood that various sizes and shapes of the threads used to tighten the skin can be utilized with the roller-structure 790, without departing from the principles of the present invention. Moreover, it will be understood that the exact sizes and shapes of the microelements and their spacings can be greatly varied when used in the roller apparatus of Figures 51 and 52, all without departing from the principles of the present invention. It should be noted that, while no openings are illustrated in detail in Figures 51 and 52, some methodology for dispensing a fluidic compound onto the skin and through the stratum corneum would be included in such a roller apparatus as illustrated at 790. Their absence on Figures 51 and 52 are solely for the purpose of clarity in these drawings.

Figures 53-58 illustrate alternative shapes of microelements that can be used in the microstructures described above. In Figure 53, a pair of pyramidal-shaped microelements 810 and 830 are illustrated as protruding from a substrate 804, and all of this is included as a microstructure, generally designated by the reference numeral 800. The two pyramidal halves 810 and 830 can be referred to as comprising a single microelement, generally designated by the reference numeral 802. The top view of Figure 54 will readily show that there is a spaced-apart relationship between the microelements-halves 810 and 830, and moreover, a slot 806 is formed in this spaced-apart area along the substrate 804. As can be seen in Figure 55, the slot 806 extends entirely through the substrate 804, thereby forming a through-slot or opening that can be used to dispense a fluidic compound, if desired.

Microelement-half 810 includes two sloped side walls 812 and 814, which are joined at a line or edge 816. This edge 816 runs between the substrate 804 and a top peak or distal point 818, which also is the intersecting point for an edge 820 that runs from the substrate 804 to this point 818, as well as a second edge 822 that runs from a different portion of the substrate 804 to the top point 818. The edges 820 and 822 are the upper boundaries of a triangular inner face or inner end wall 824.

Microelement-half 830 includes two sloped side walls 832 and 834, which are joined at a line or edge 836. This edge 836 runs between the substrate 804 and a top peak or distal point 838, which also is the intersecting point for an edge 840 that runs from the substrate 804 to this point 838, as well as a second edge 842 that runs from a different portion of the substrate 804 to the top point 838. The edges 840 and 842 are the upper boundaries of a triangular inner face or inner end wall 844. Since the edges 816 and 836 are substantially sharp, the microelement 802 will readily penetrate into the skin and through the stratum corneum layer when this microelement is moved in either direction "C" as indicated by the arrow on Figure 54.

Figures 56-58 illustrate another alternative embodiment for a microelement that comprises two half-structures, similar to that described in reference to Figures 53-55. The overall structure is generally designated by the reference numeral 850, which includes a substrate 854, a first wedge-shaped microstructure 860, a second wedge-shaped microstructure 880, and a through-slot 856. Moreover, the two microelement-halves 860 and 880 can be, in combination, referred to as a single microelement 852.

The microelement-half 860 comprises a wedge-shaped structure that has a triangular shape when viewed from above (see Figure 57). The side walls of this structure 860 are designated at the reference numerals 862 and 864, as well as an inner or end wall at 874. The top surface is designated by the reference numeral 868.

The two side walls 862 and 864 come together at a substantially sharp edge 866, which extends from the substrate 854 to the top surface 868. The side wall 862 and the inner end wall or face 874 come together at an edge 870, which extends from the substrate 854 to the top surface 868. The side wall 864 and the inner wall or face 874 also come together at an edge 872, which extends from the substrate 854 to the top surface 868.

The microelement-half 880 comprises a wedge-shaped structure that has a triangular shape when viewed from above (see Figure 57). The side walls of this structure 880 are designated at the reference numerals 882 and 884, as well as an inner or end wall at 894. The top surface is designated by the reference numeral 888.

The two side walls 882 and 884 come together at a substantially sharp edge 886, which extends from the substrate 854 to the top surface 888. The side wall 882 and the inner end wall or face 894 come together at an edge 890, which extends from the substrate 854 to the top surface 888. The side wall 884 and the inner wall or face 894 also come together at an edge 892, which extends from the substrate 854 to the top surface 888.

As can be seen in Figure 58, the opening 856 runs completely through the substrate 854, thereby forming a through-hole or through-slot that will allow a fluidic material to pass therethrough. Since the edges 866 and 886 are substantially sharp, the microelement 852 will readily penetrate into the skin and through the stratum corneum layer when this microelement is moved in either direction "C" as indicated by the arrow on Figure 57. Of course, the other edges 870, 872, 890, and 892 could also be made to be substantially sharp, so that, if desired, the microelement 852 would also readily penetrate skin through the stratum corneum layer if the microelement were moved in a direction perpendicular to the arrows "C."

The foregoing description of a preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise form disclosed. Obvious modifications or variations are possible in light of the above teachings. The embodiment was chosen and described in order to best illustrate the principles of the invention and its practical application to thereby enable one of ordinary skill in the art to best utilize the invention in various embodiments and with various modifications as are suited to the particular use contemplated. It is intended that the scope of the invention be defined by the claims appended hereto.

THE INVENTION CLAIMED IS:

1. A rotatable microstructure apparatus, characterized in that it comprises: a roller structure which includes a curved substrate and a plurality of microelements affixed upon a first surface of said substrate; said plurality of microelements being of predetermined sizes and shapes so as to penetrate a stratum corneum layer of skin when said microstructure apparatus is placed upon said skin and rolled over said skin in at least one predetermined direction.

2. The rotatable microstructure apparatus as recited in claim 1, wherein a shape of at least one of the plurality of microelements exhibits a directional orientation, such that said directional orientation facilitates the penetration of the skin when movement of the microstructure apparatus occurs in said at least one predetermined direction.

3. The rotatable microstructure apparatus as recited in claim 2, wherein said shape of at least one of the plurality of microelements comprises one of: (a) a three-sided pyramid extending from said substrate first surface, in which two sides each form a right triangle with said substrate, and their hypotenuses meet at an edge, a third side which forms an isosceles triangle, and wherein all three sides meet at a peak that is distal from said substrate first surface, wherein said peak and third side form a directional cutting surface; (b) a three-sided pyramid extending from said substrate first surface, in which two sides each form a triangle with said substrate, and their hypotenuses meet at an edge, a third side which forms an isosceles triangle, said two sides exhibit an acute angle with said substrate first surface proximal to said third side, and wherein all three sides meet at a peak that is distal from said substrate first surface, wherein said peak and third side form a directional cutting surface; and (c) a three-sided pyramid extending from said substrate first surface, in which two sides each form a triangle with said substrate, and their hypotenuses meet at an edge, a third side which forms an isosceles triangle, said two sides exhibit an obtuse angle with said substrate first surface proximal to said third side, and wherein all three sides meet at a peak that is distal from said substrate first surface, wherein said peak and third side form a directional cutting surface

4. The rotatable microstructure apparatus as recited in any of claims 1-3, wherein said roller structure comprises a substantially cylindrical surface that is in mechanical communication with an axle which supports said roller structure.

5. The rotatable microstructure apparatus as recited in any of claims 1-4, further comprising: a hand-held body containing at least one axle, said axle providing support for said roller structure.

6. The rotatable microstructure apparatus as recited in any of claims 1-5, further comprising: at least one chamber located on a second surface of said substrate that is opposite from said first surface, and a fluidic compound that flows through at least one passageway between said first and second surfaces of said substrate.

7. The rotatable microstructure apparatus as recited in claim 6, wherein said at least one passageway comprises one of: (a) an opening in at least one of said microelements, and (b) a through-hole in said substrate.

8. A method for reducing the barrier properties of skin, the method characterized in that it comprises:

(a) providing a rotatable microstructure having a curved substrate and a plurality of microelements that protrude from said curved substrate by at least one predetermined protrusion distance; and

(b) placing and rolling the rotatable microstructure on a surface of skin, wherein said at least one predetermined protrusion distance is sufficient so that many of said plurality of microelements penetrate a stratum corneum layer of said skin.

9. The method as recited in claim 8, further comprising the step of: providing at least one chamber located within said curved substrate; and dispensing a fluidic compound that flows through at least one passageway from said at least one chamber,

thereby both penetrating said skin and delivering said fluidic compound to said skin in a single procedure.

10. The method as recited in claim 8 or 9, further comprising the step of: providing a hand-held body containing at least one axle, said axle providing support for said rotatable microstructure.

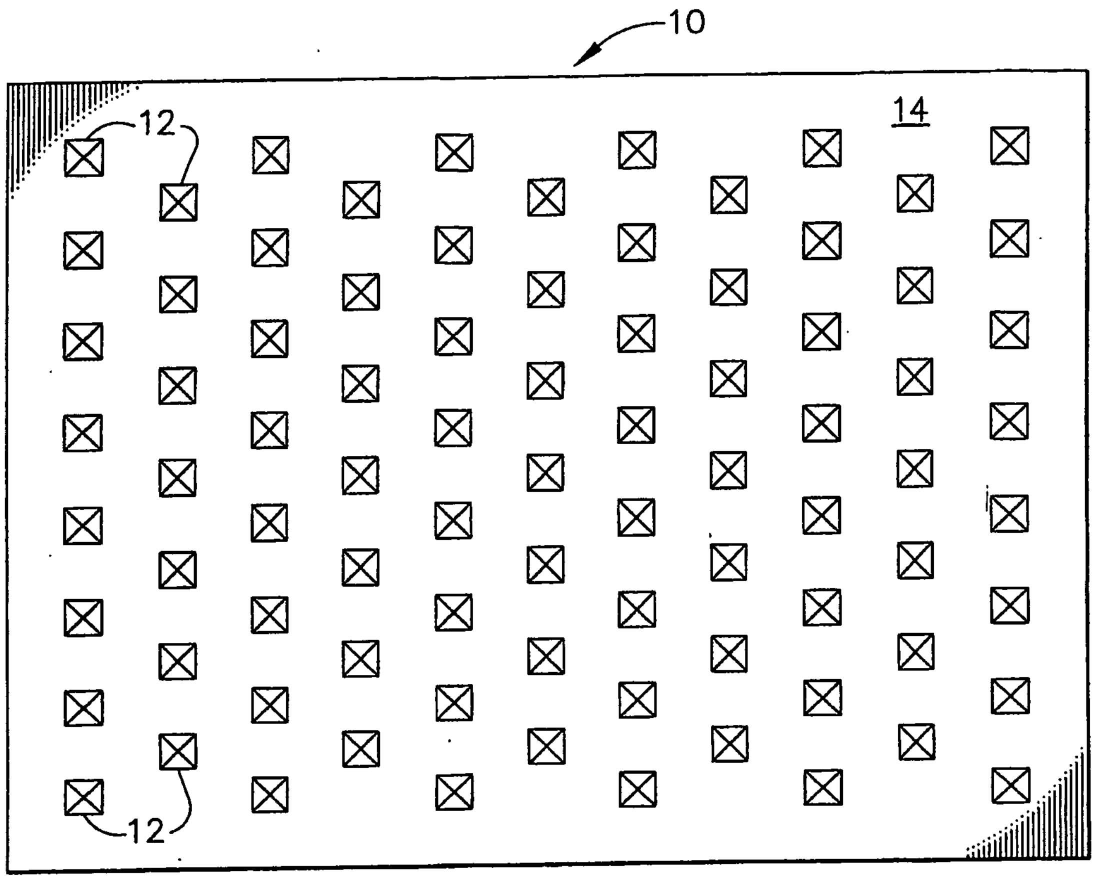

FIG. 1

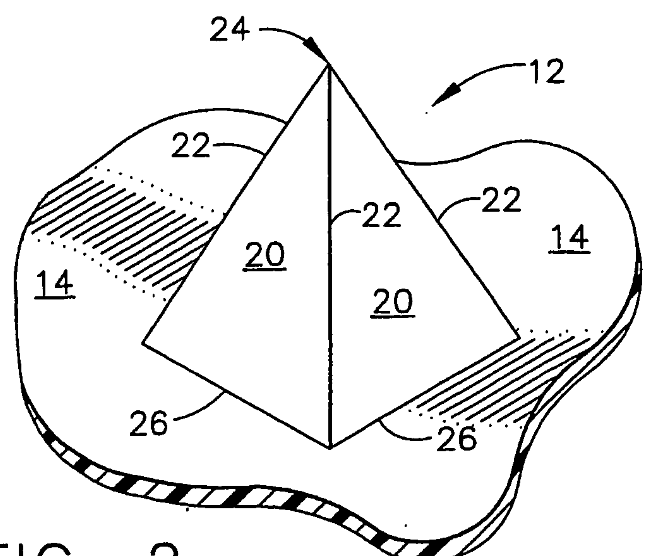

FIG. 2

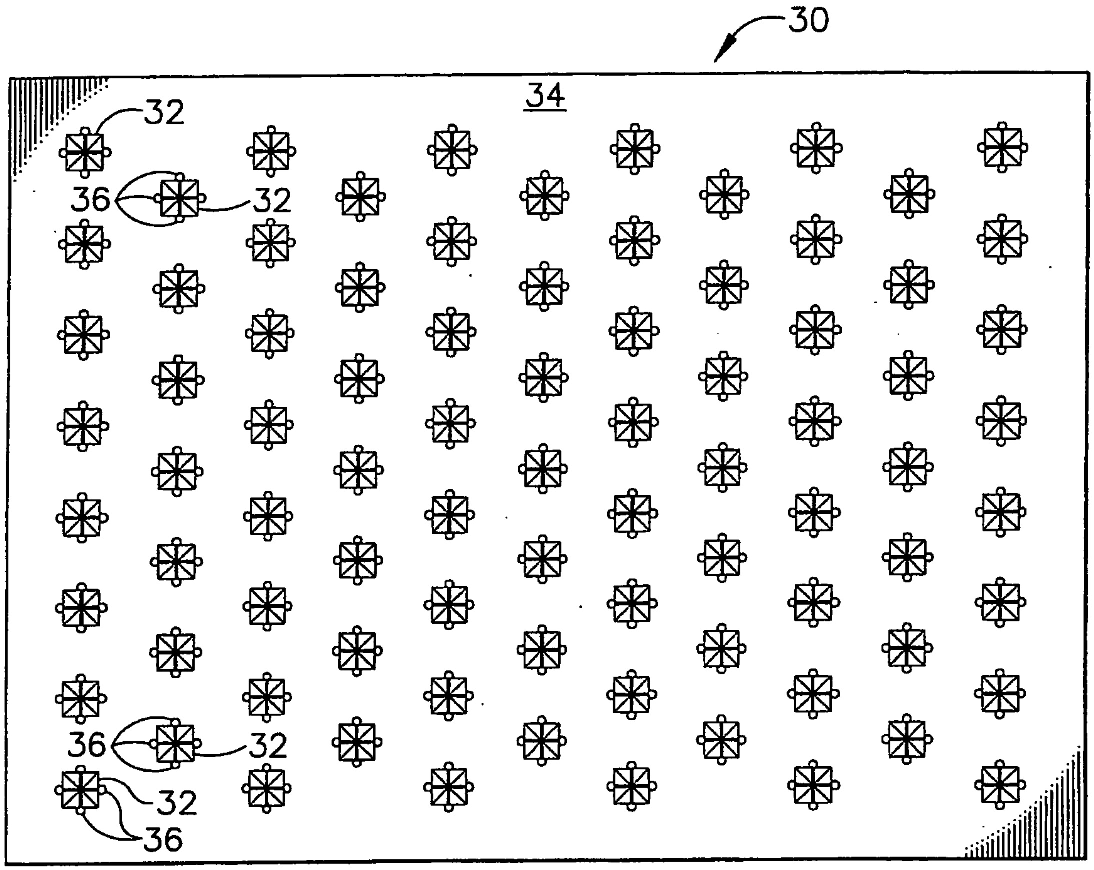
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FIG. 3

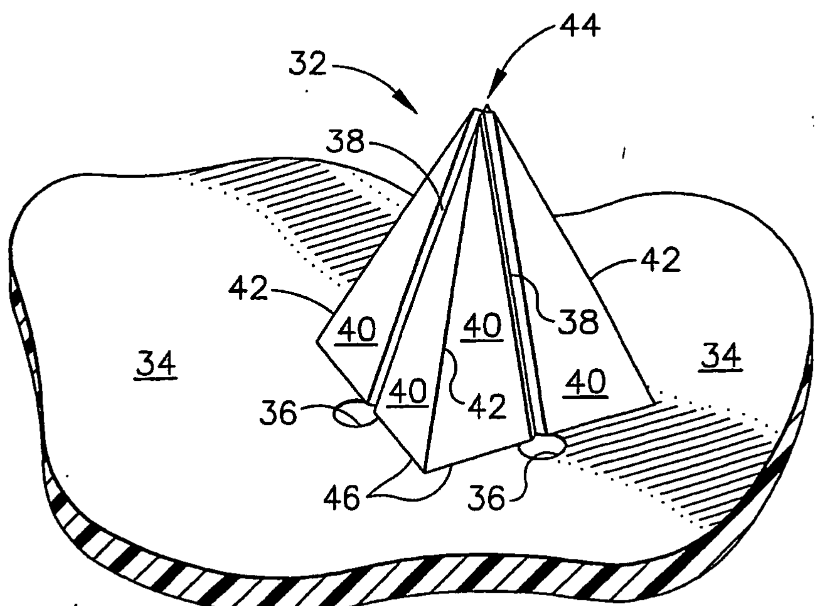
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FIG. 4

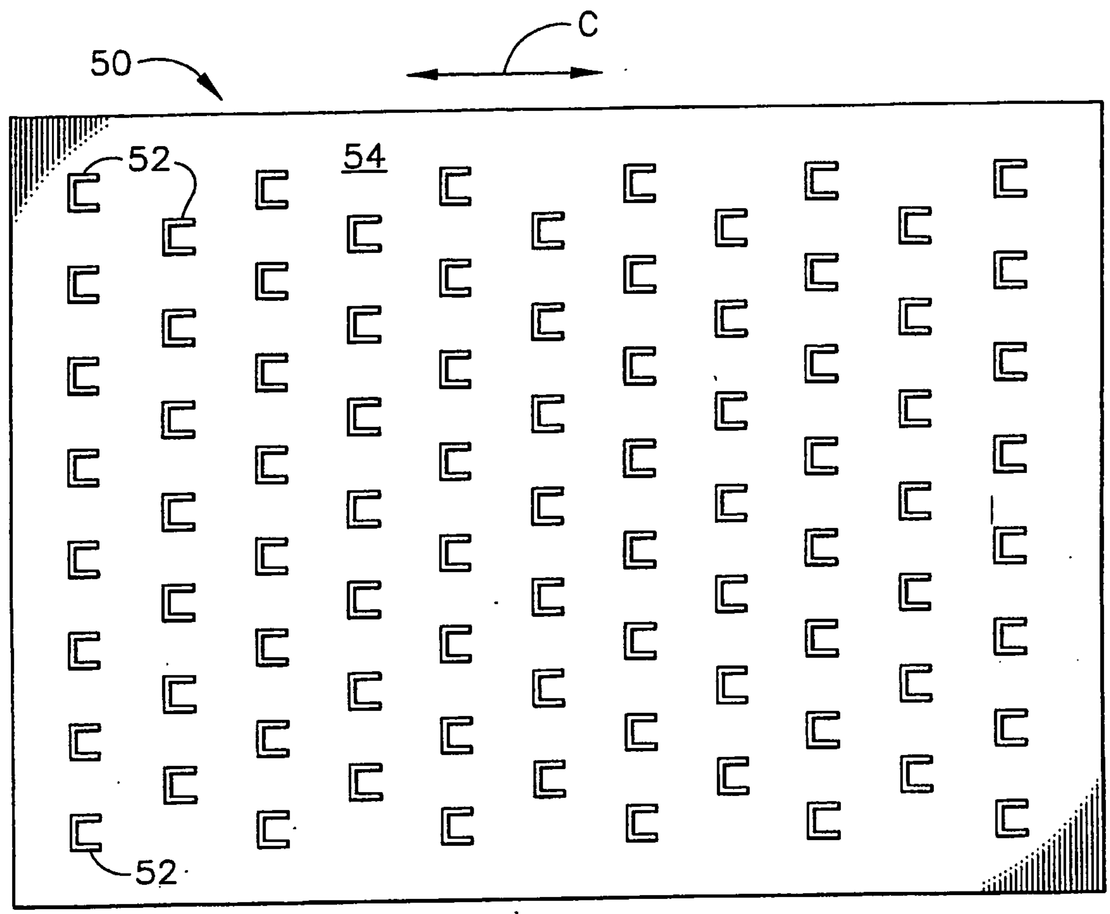


FIG. 5

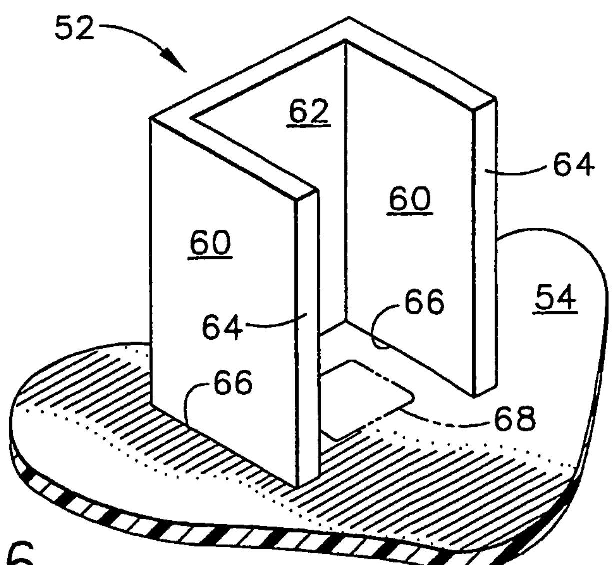


FIG. 6

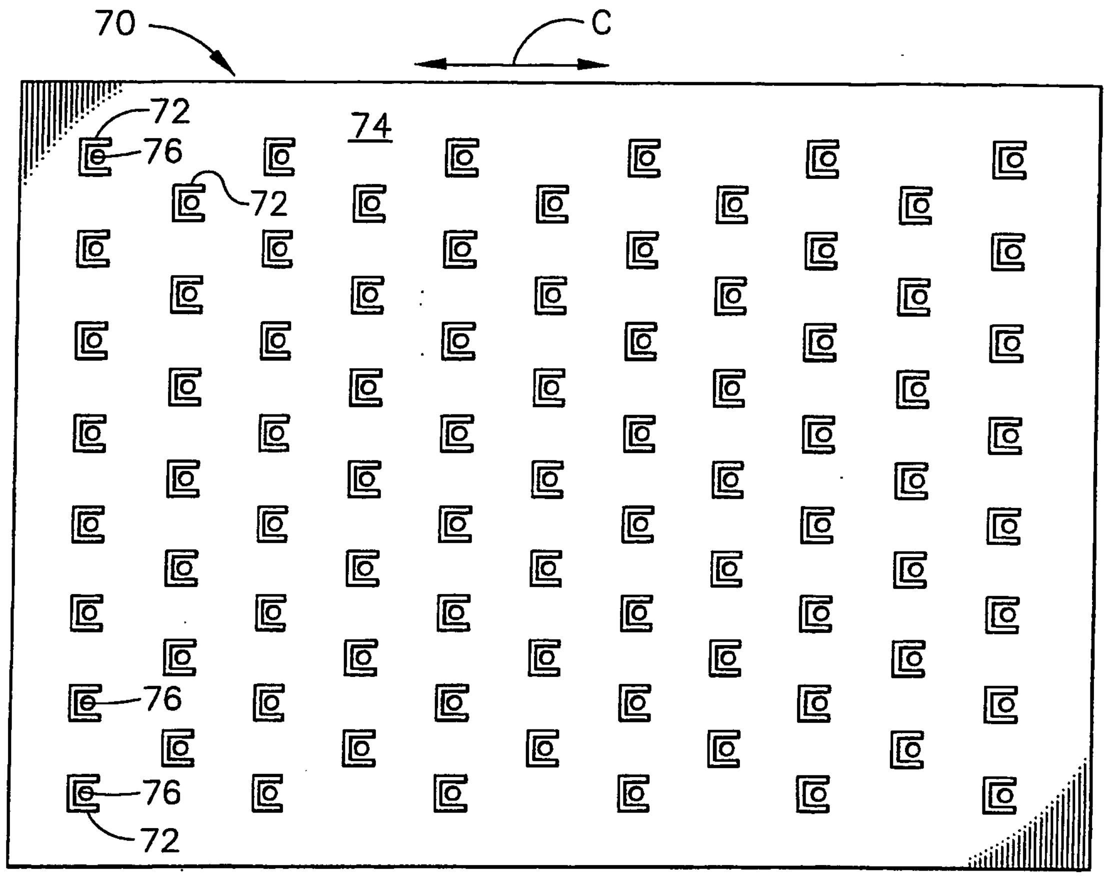


FIG. 7

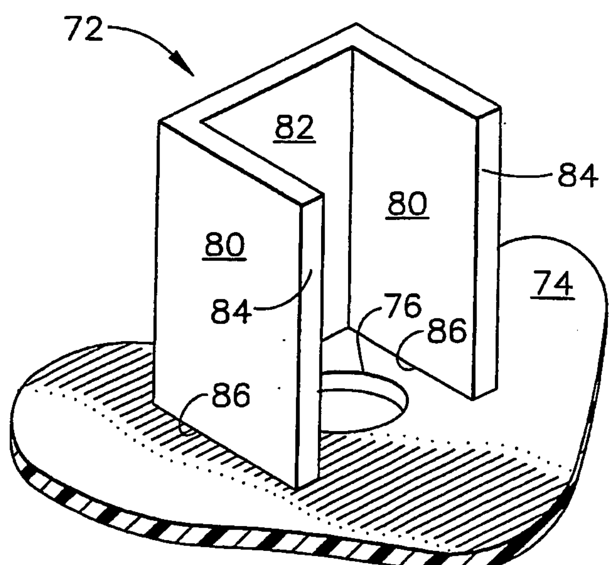


FIG. 8

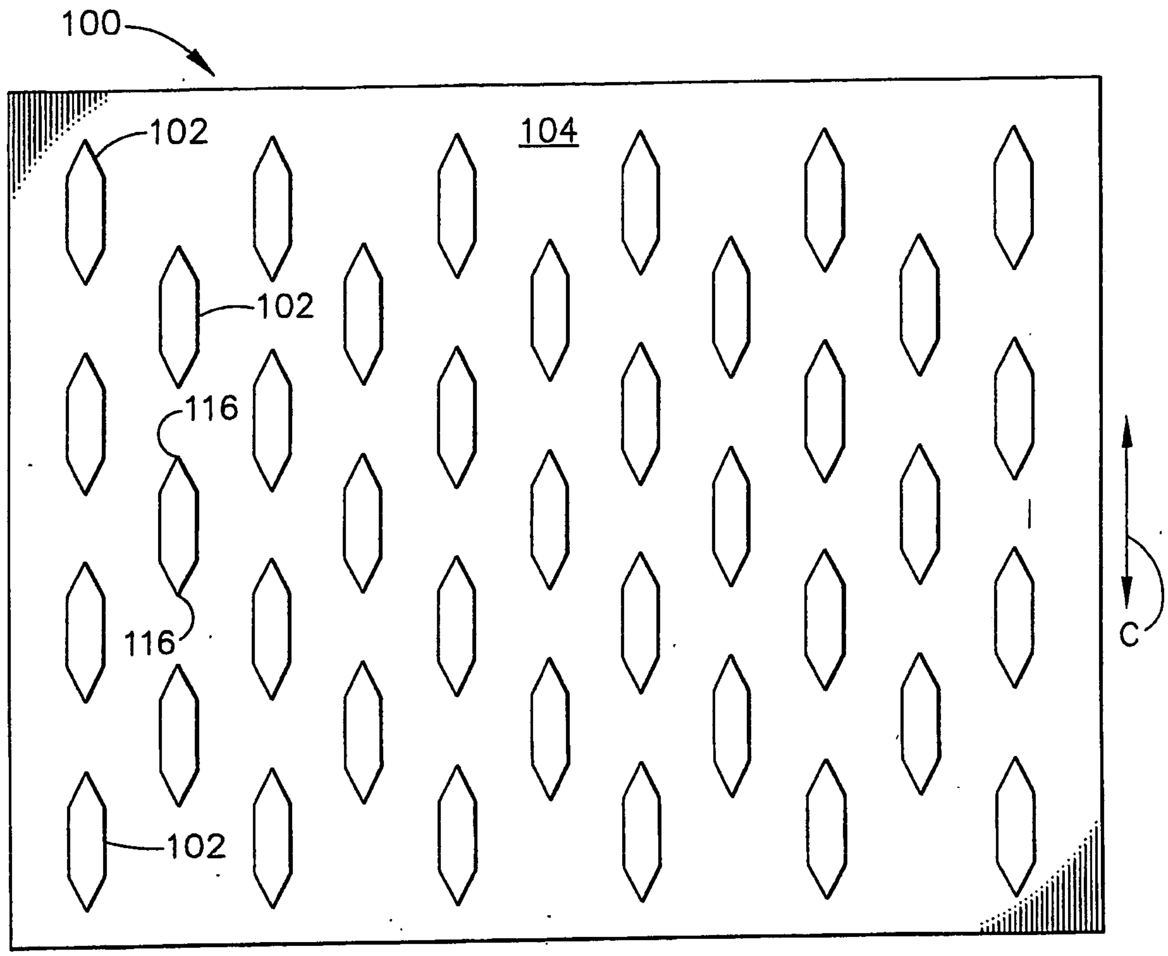


FIG. 9

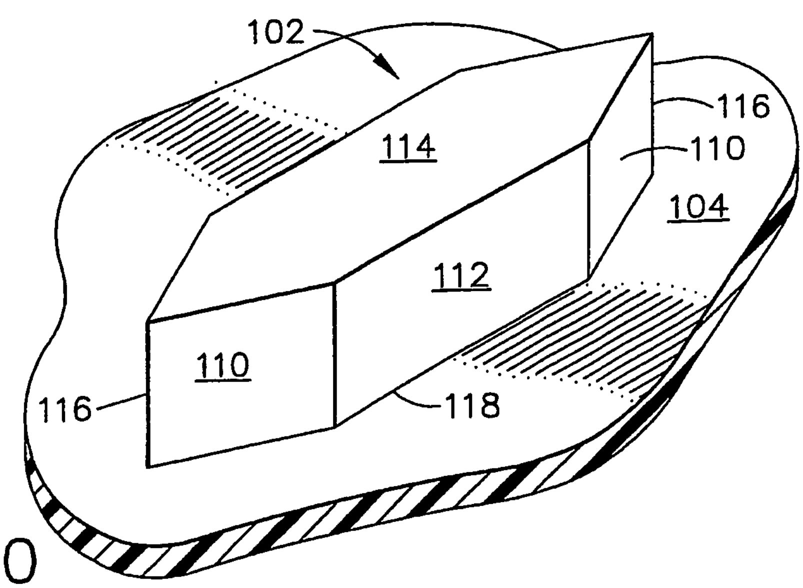
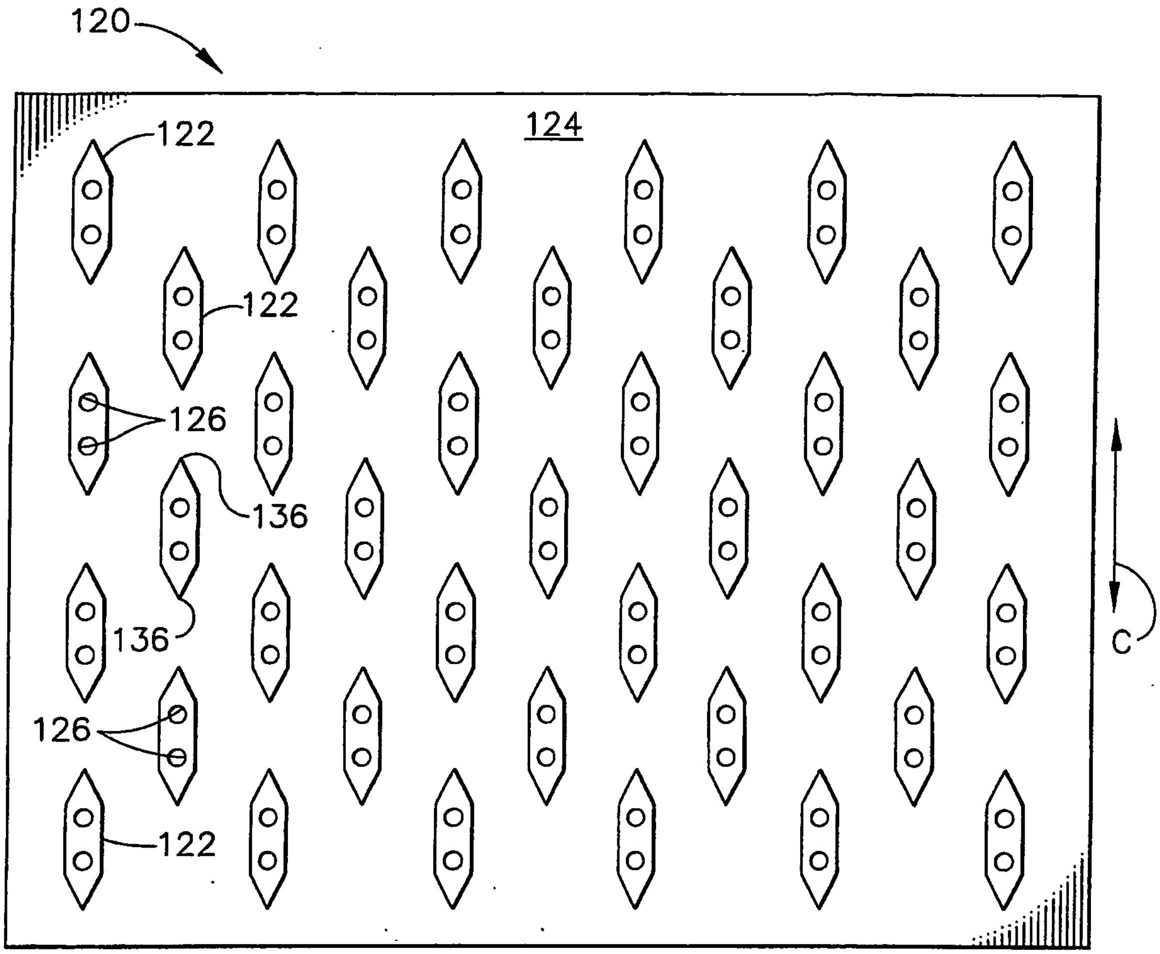


FIG. 10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122
C

FIG. 11

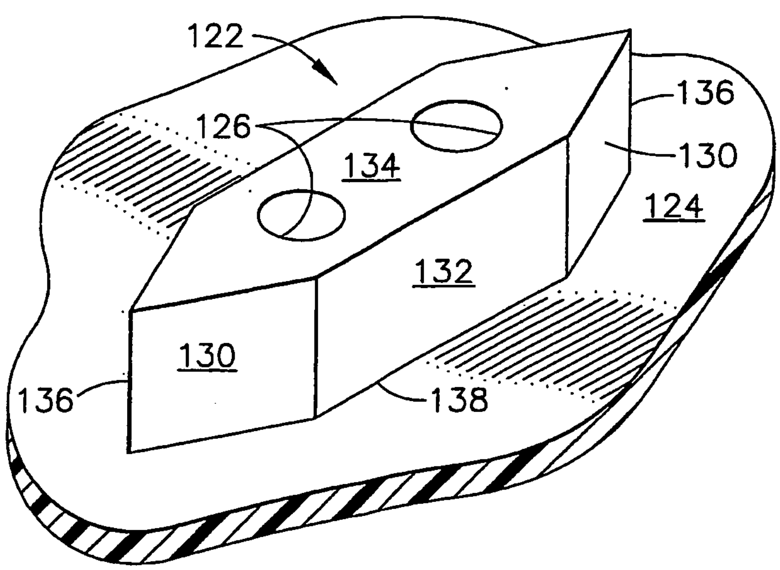
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FIG. 12

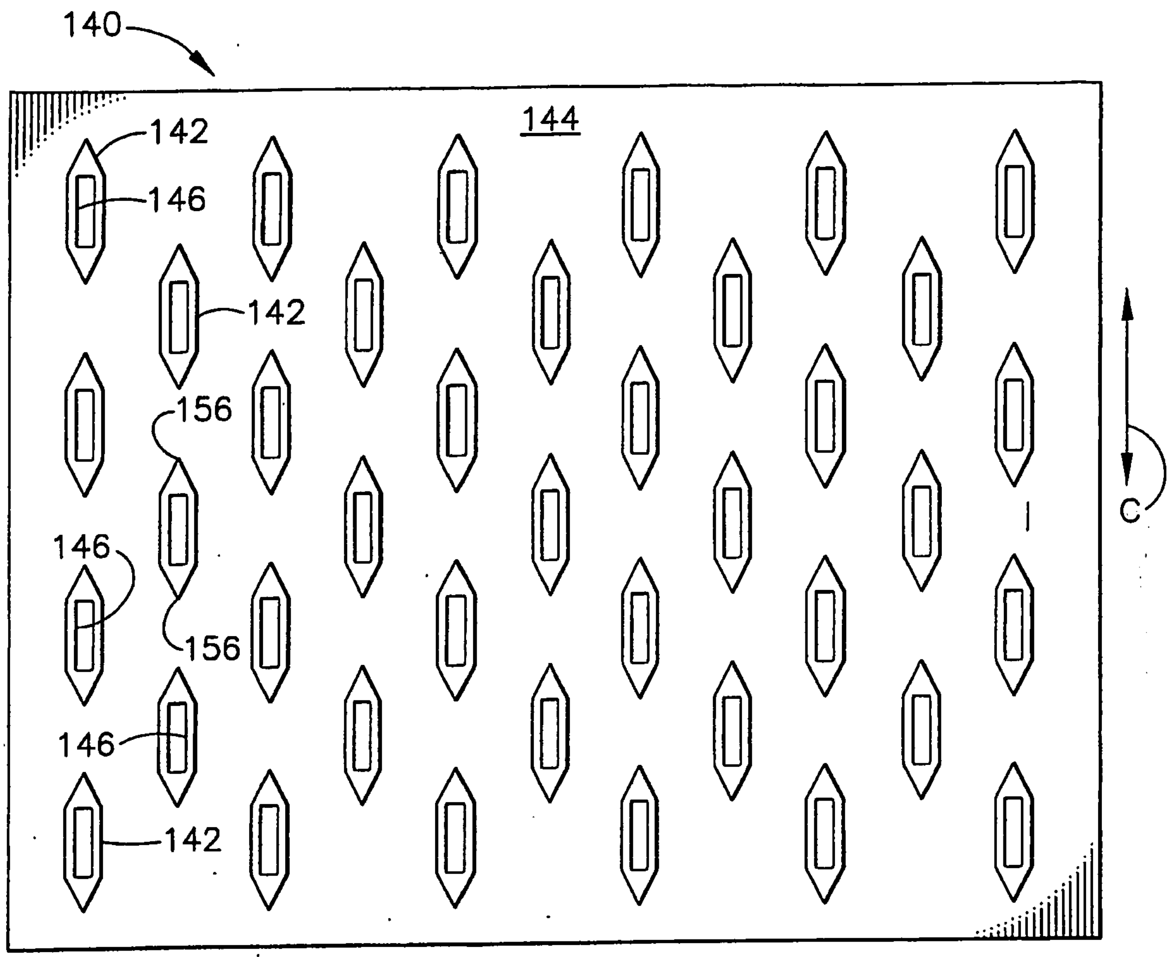
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FIG. 13

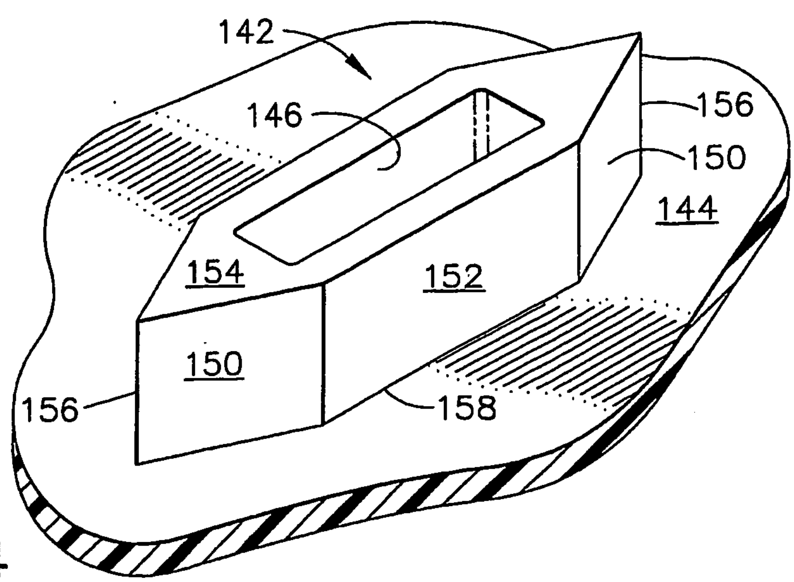
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FIG. 14

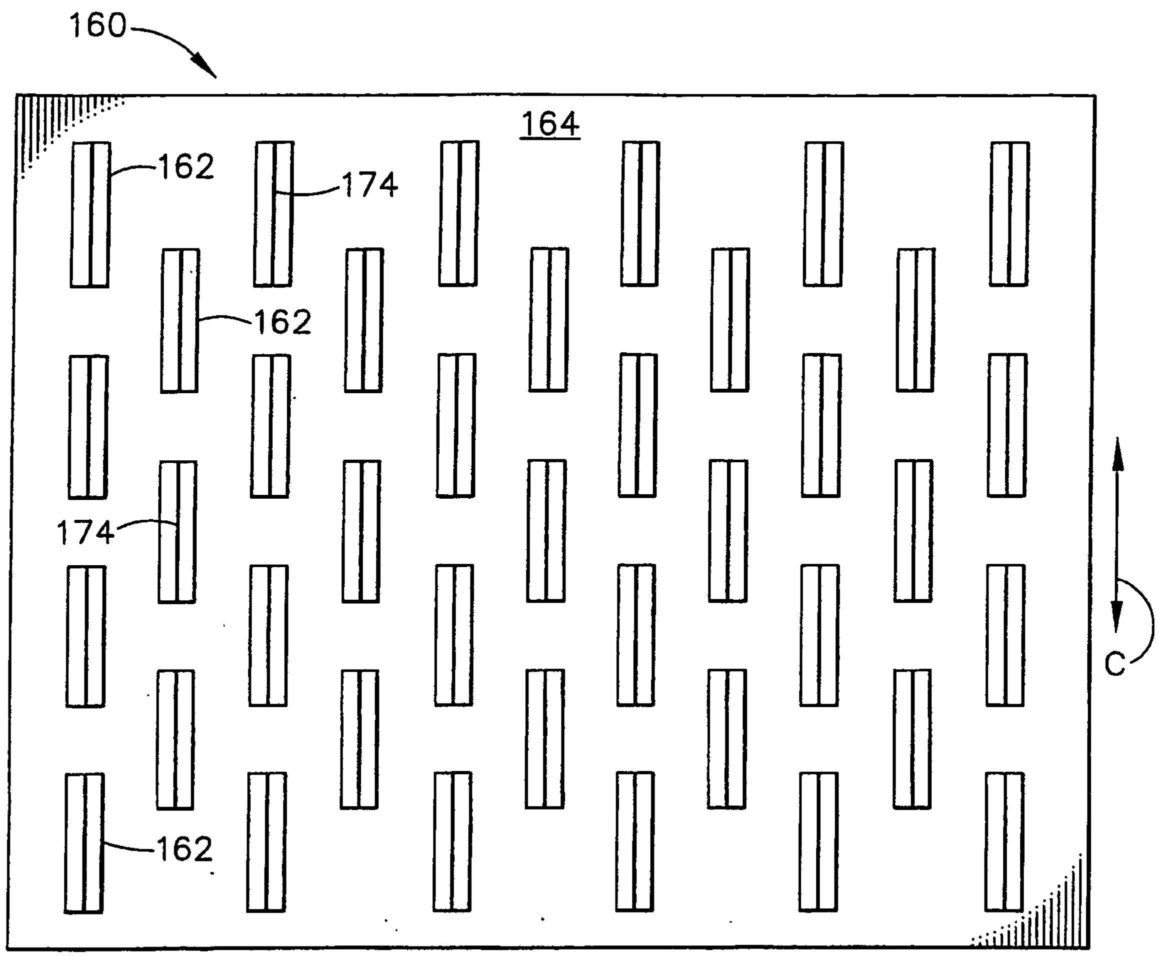

FIG. 15

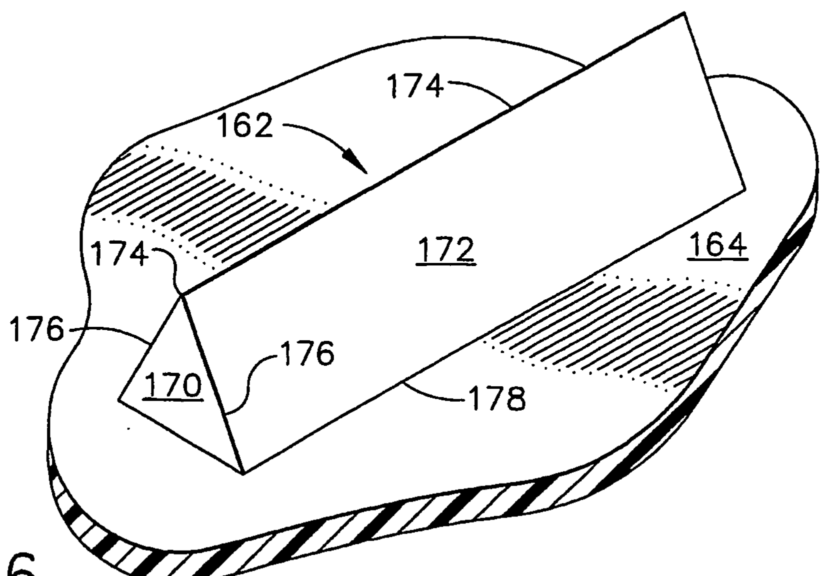

FIG. 16

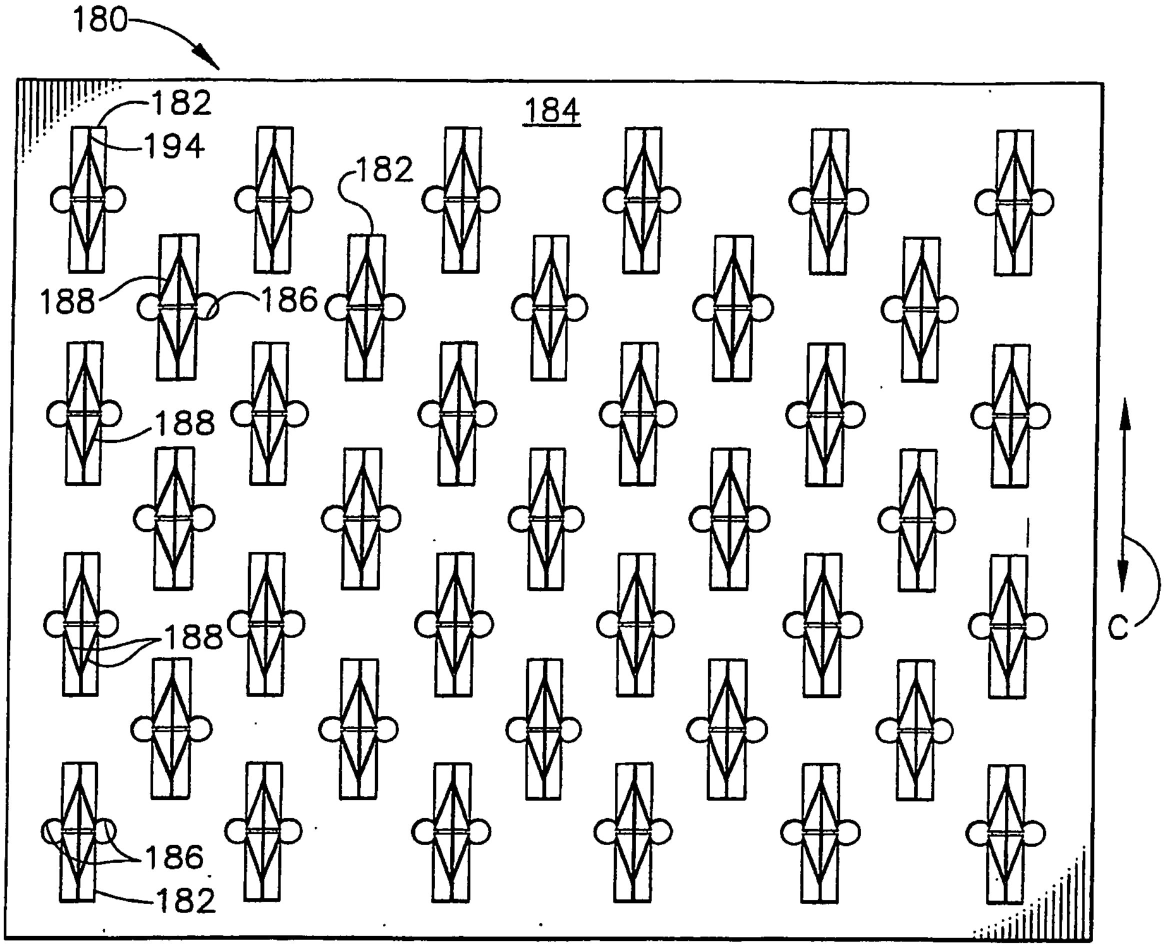
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FIG. 17

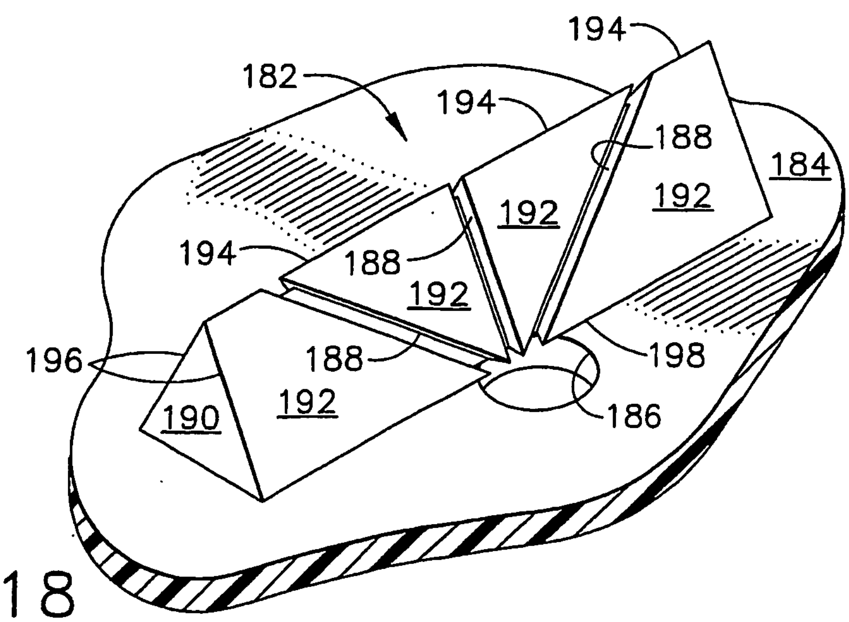
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FIG. 18

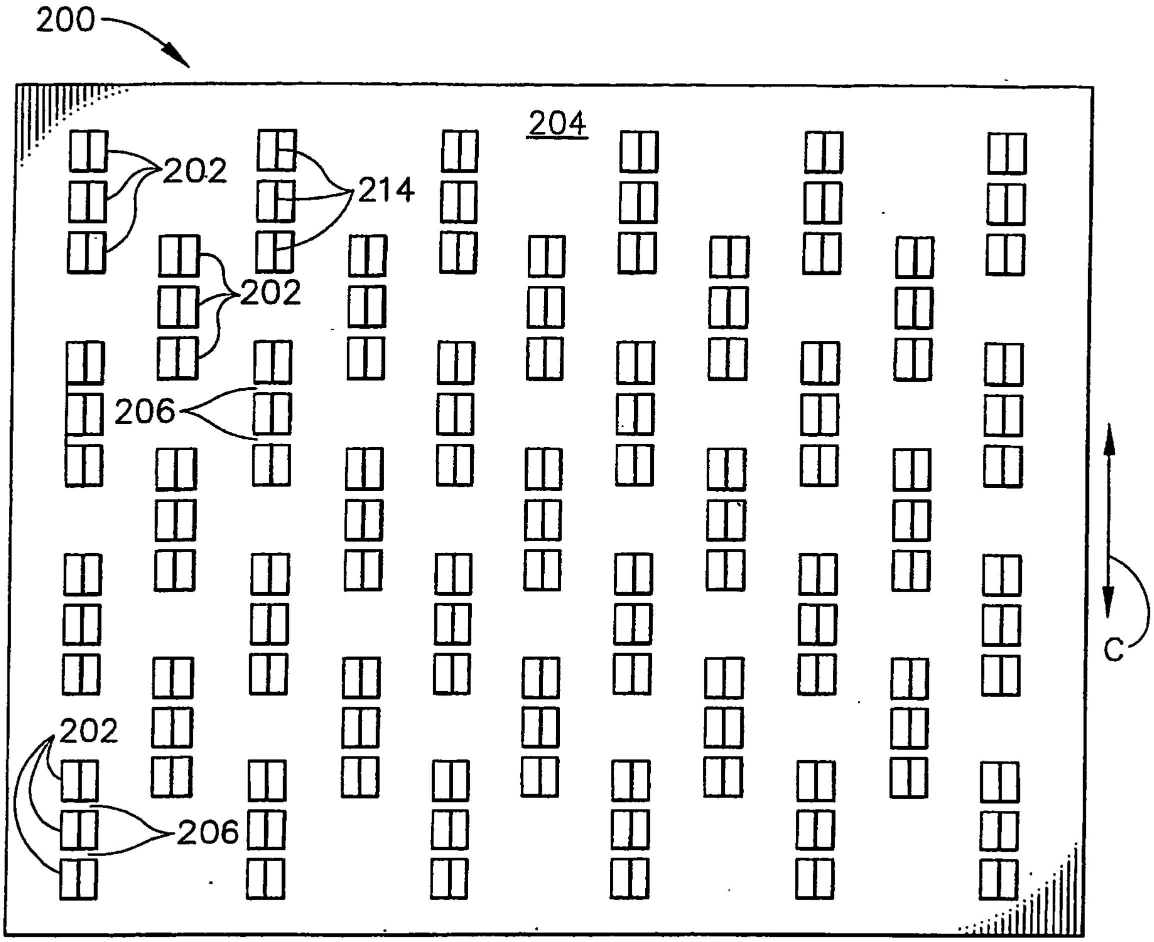
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FIG. 19

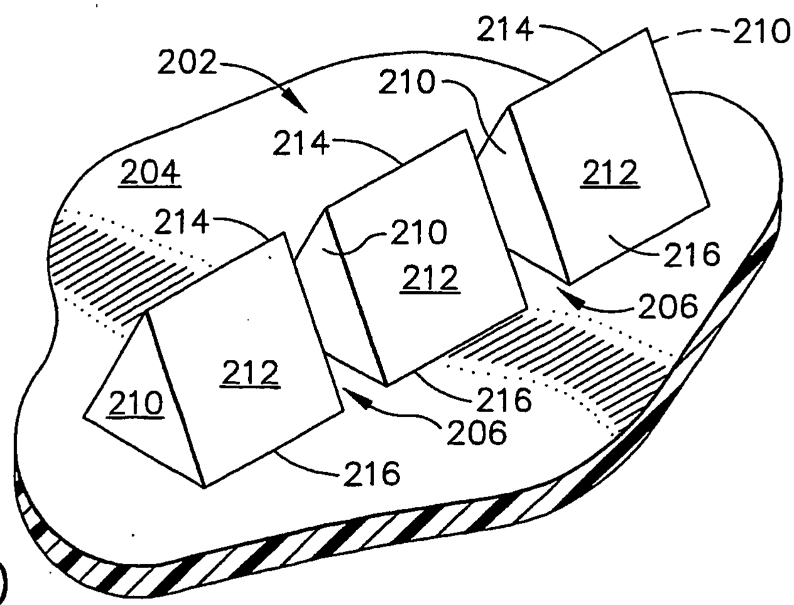
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FIG. 20

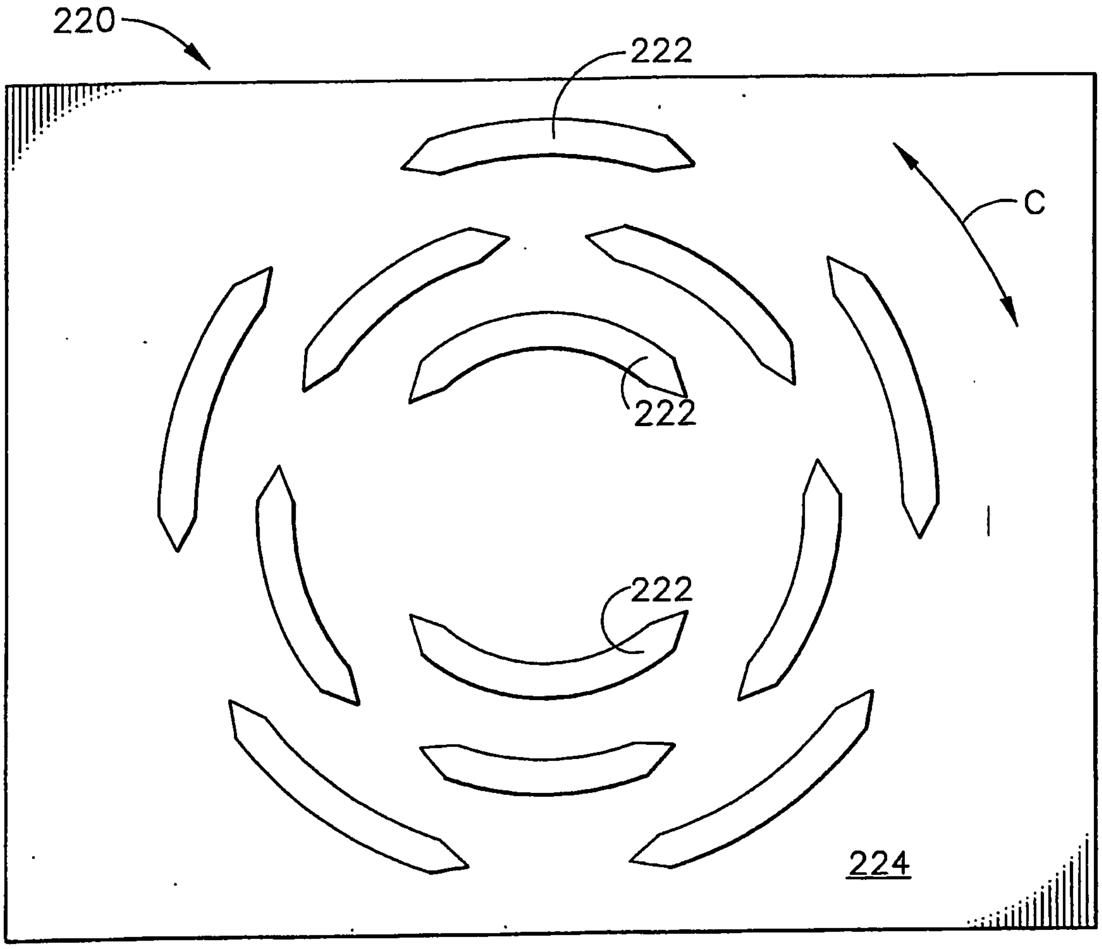

FIG. 21

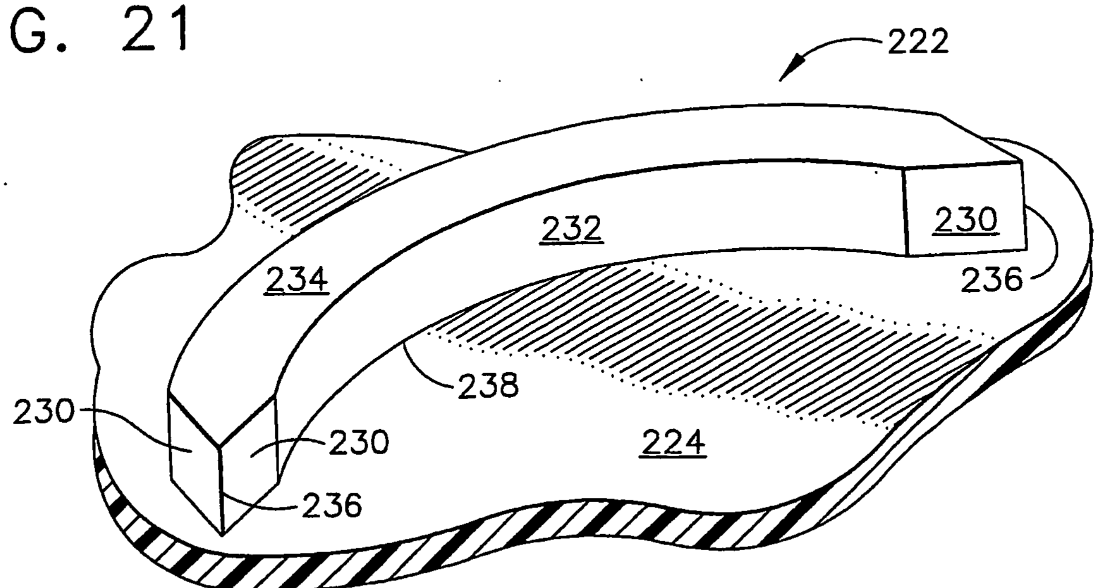

FIG. 22

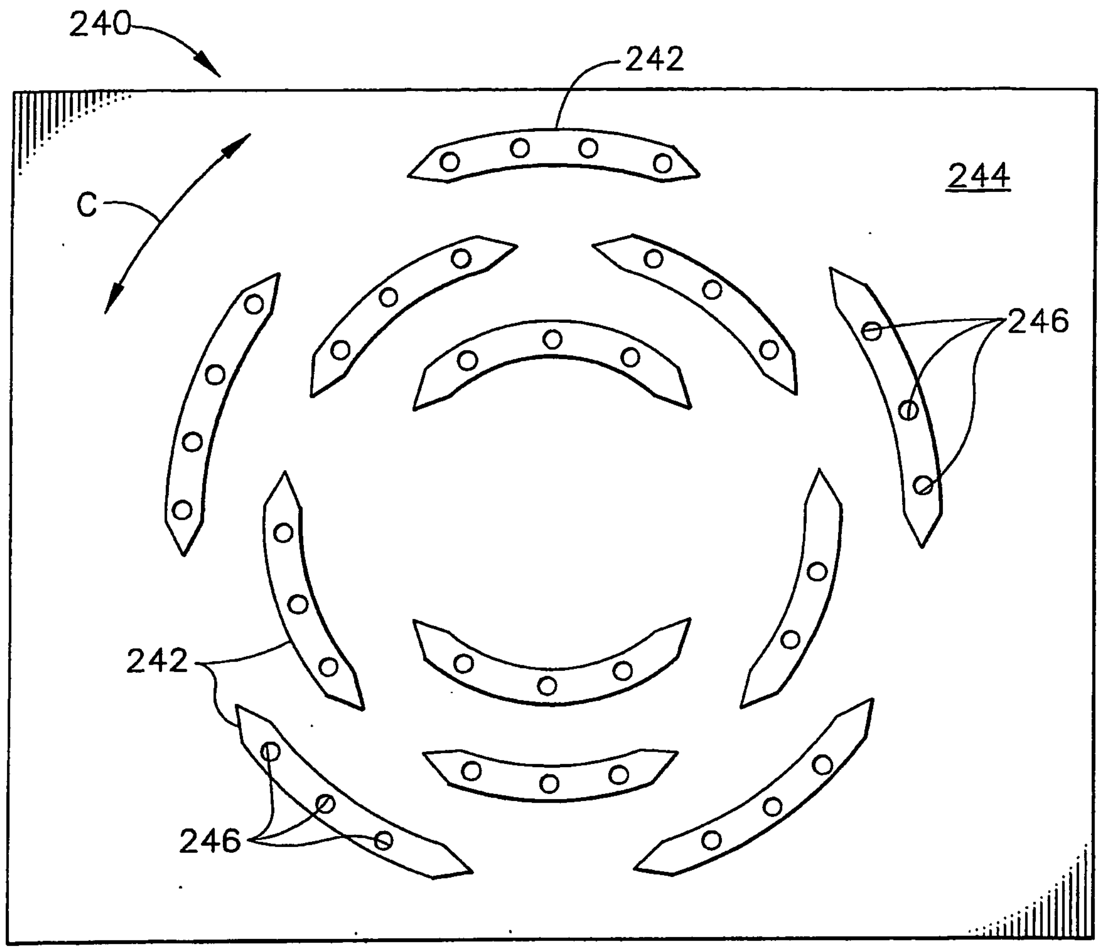
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FIG. 23

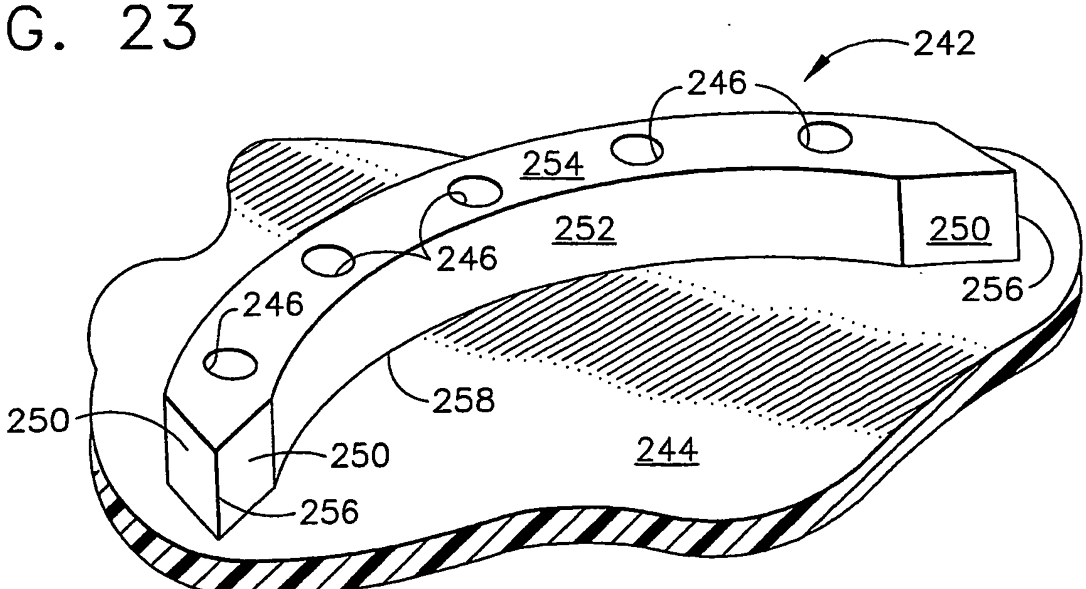
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FIG. 24

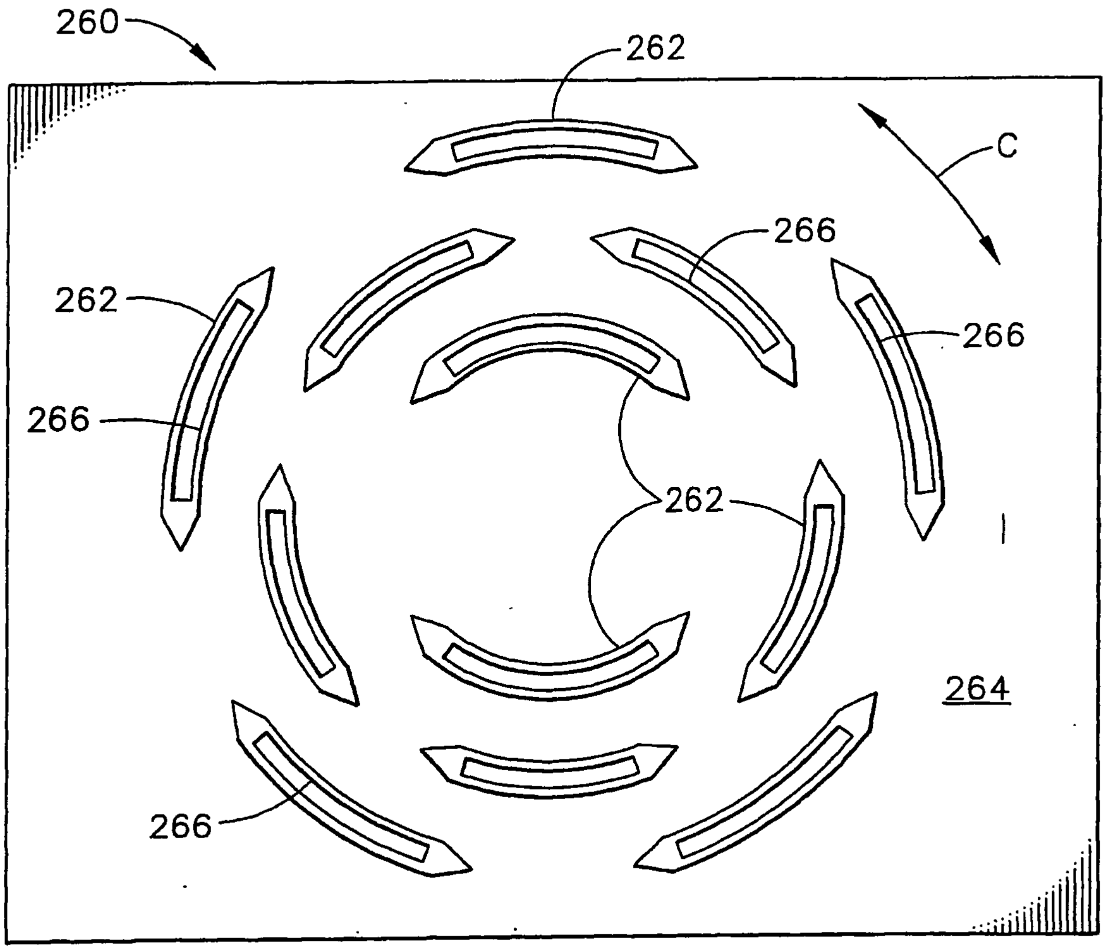
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FIG. 25

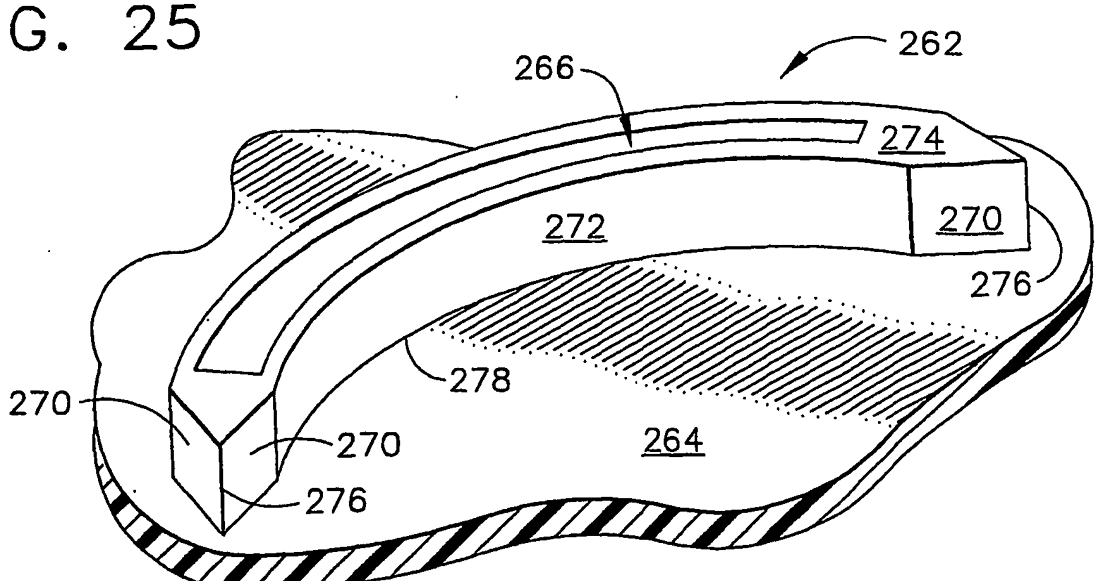
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FIG. 26

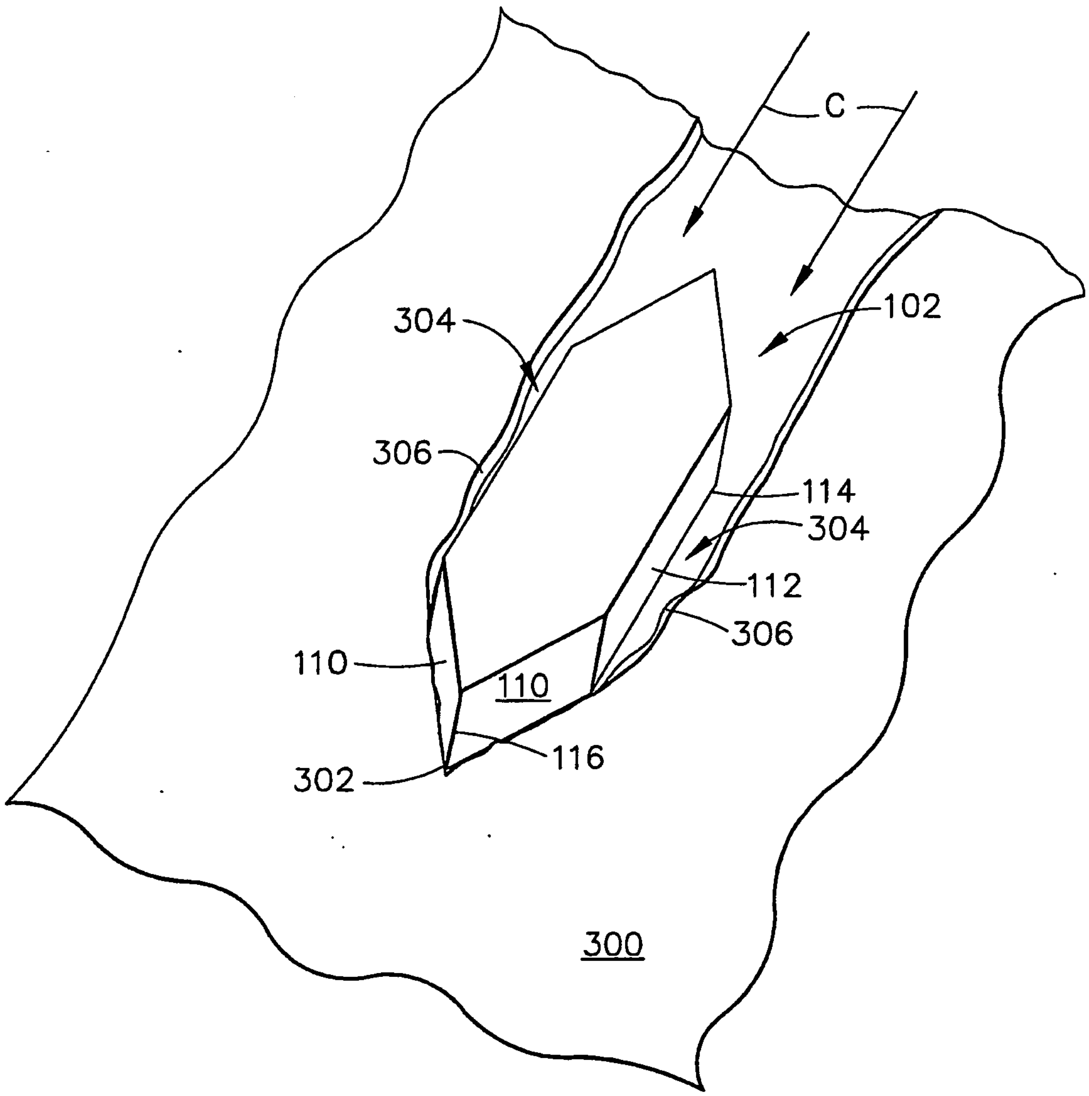

FIG. 27

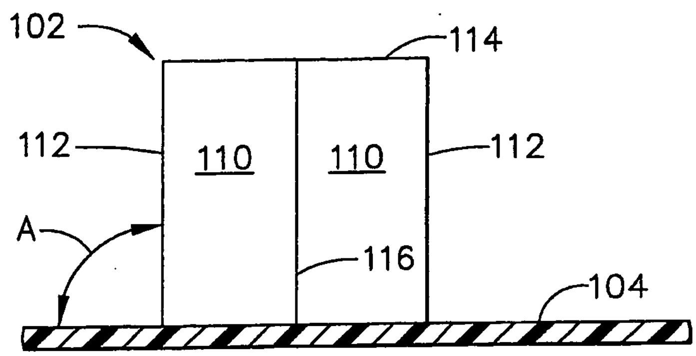
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FIG. 28

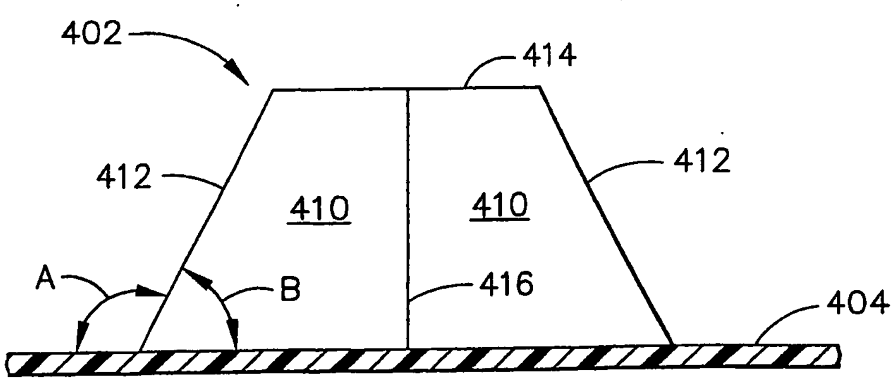
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FIG. 29

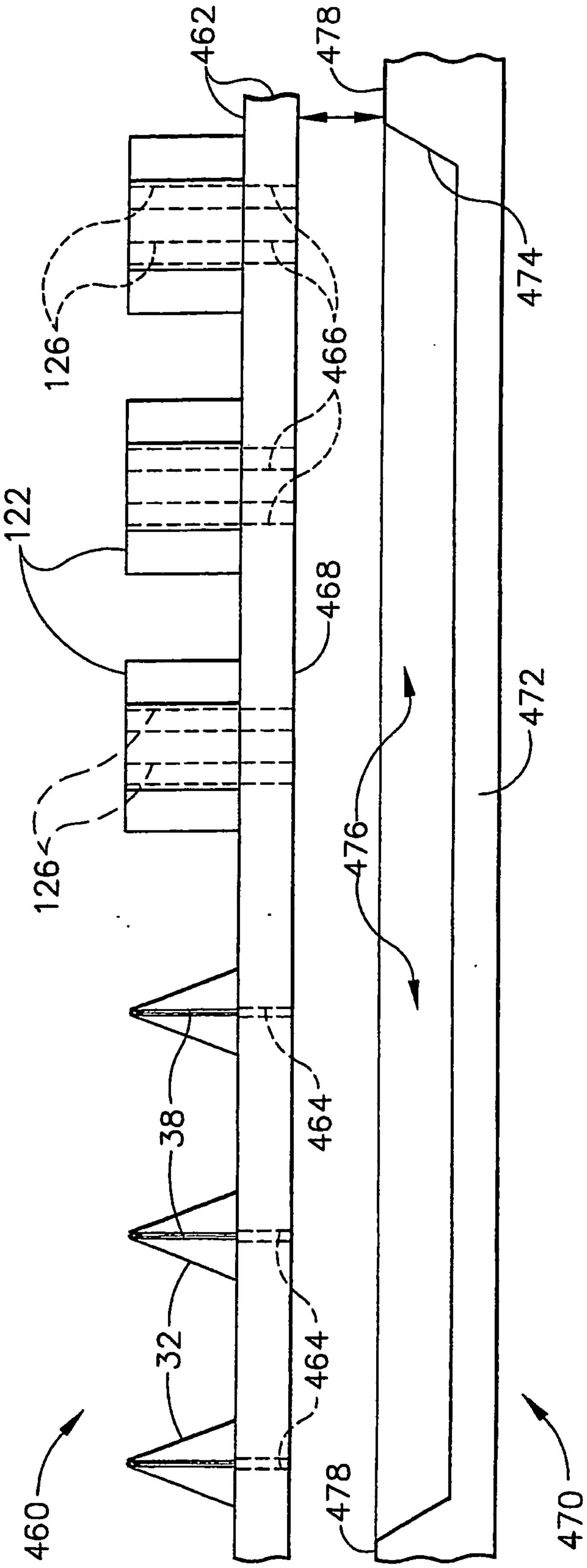


FIG. 30

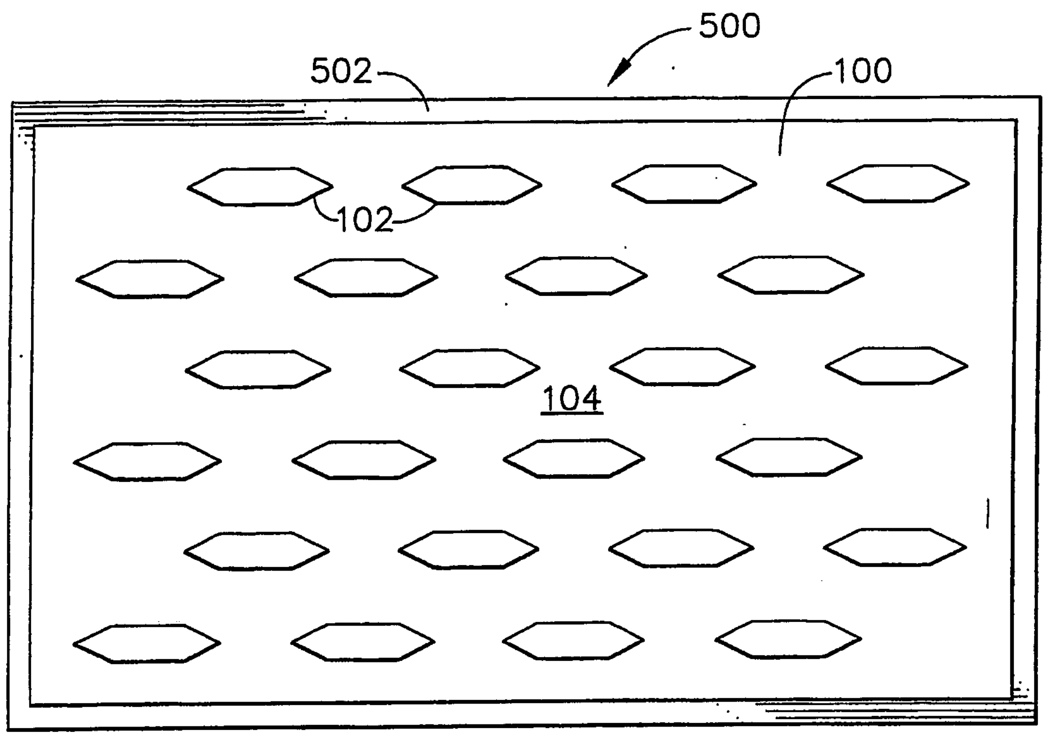


FIG. 31

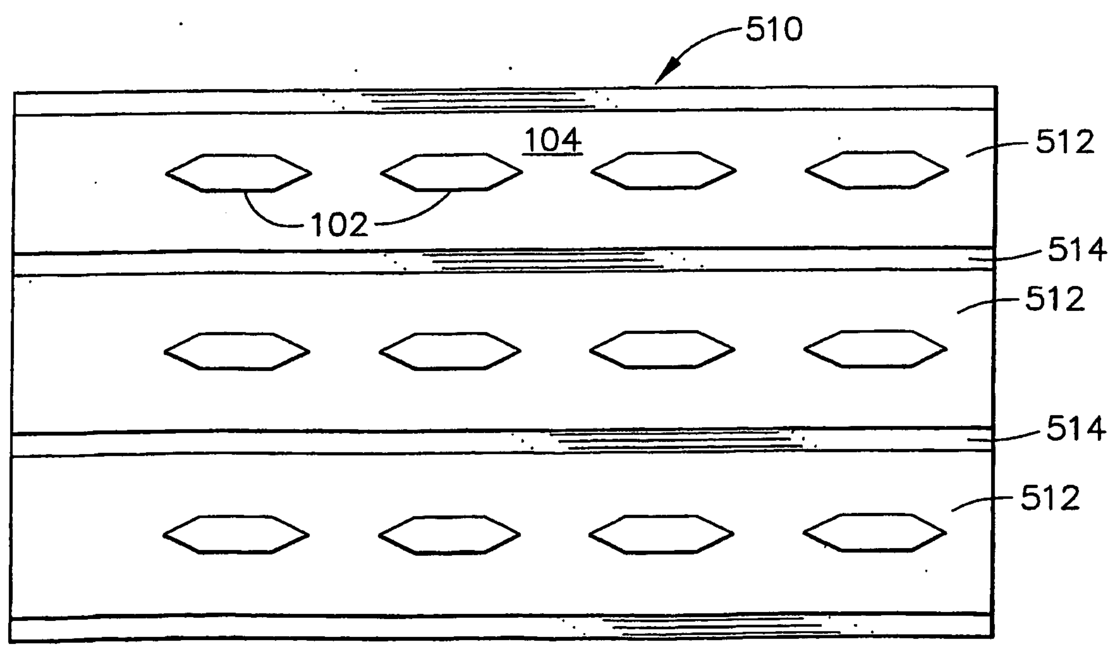


FIG. 32

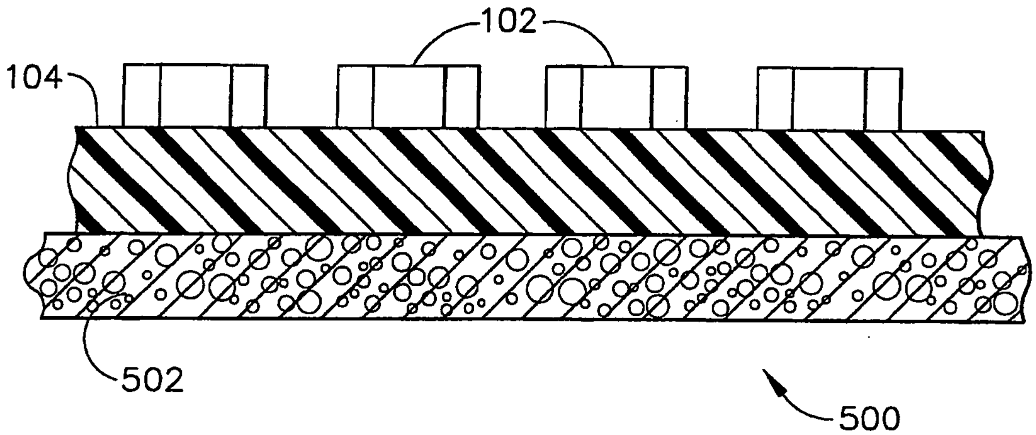


FIG. 33

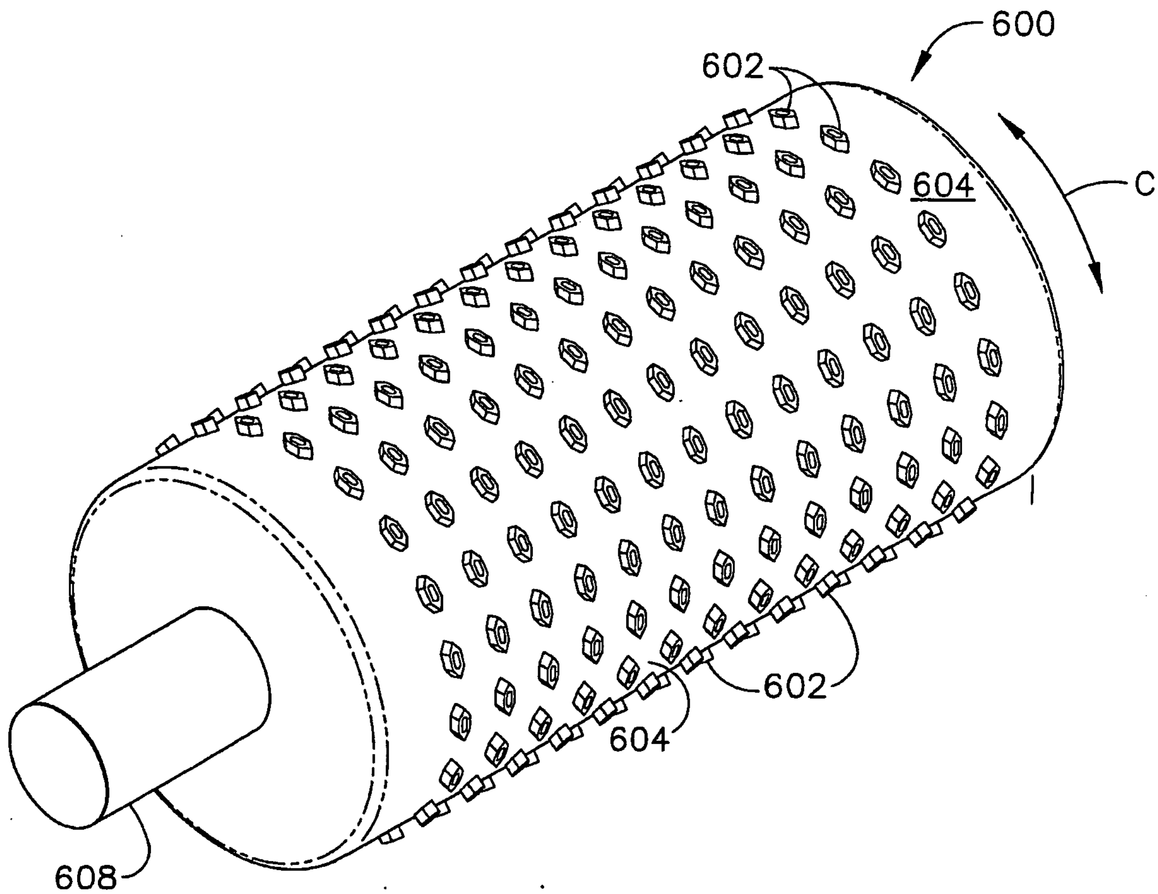


FIG. 34

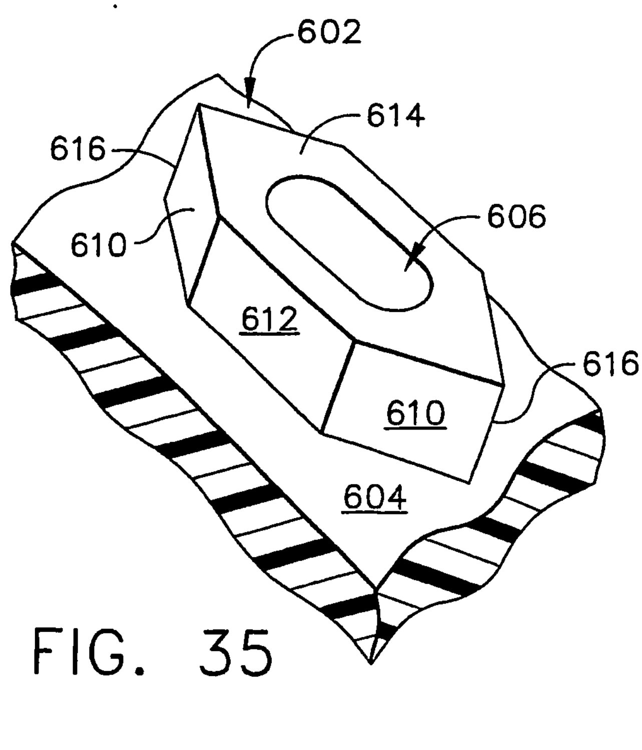


FIG. 35

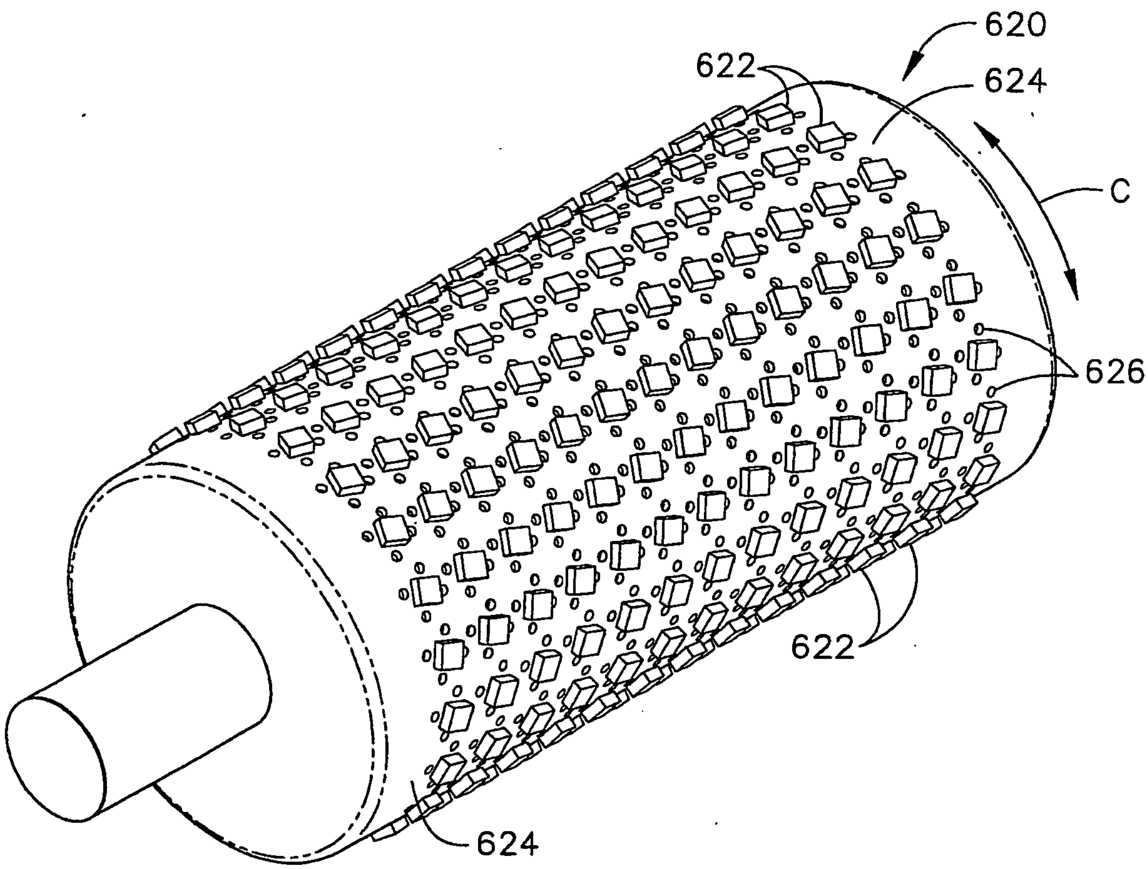


FIG. 36

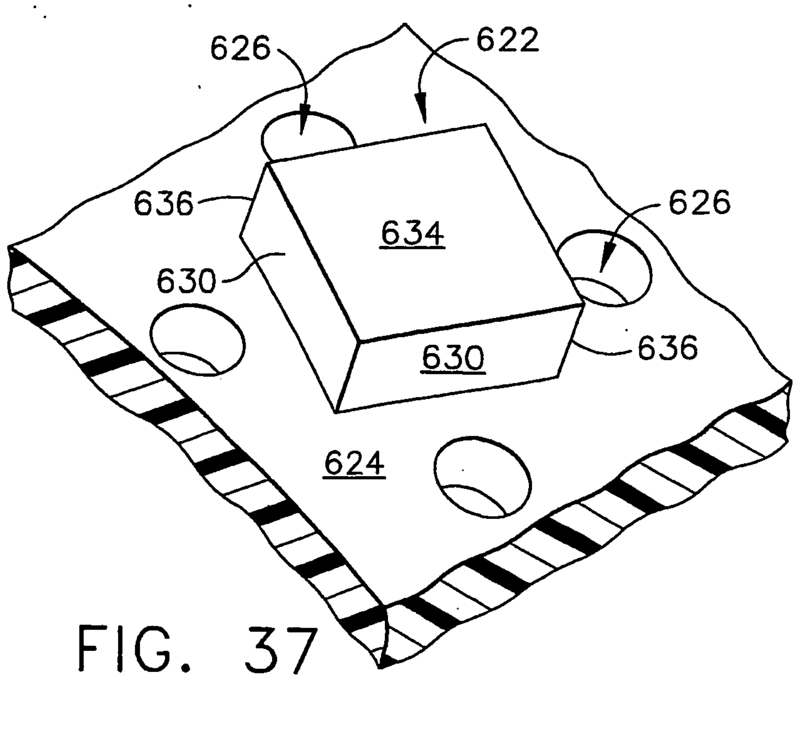


FIG. 37

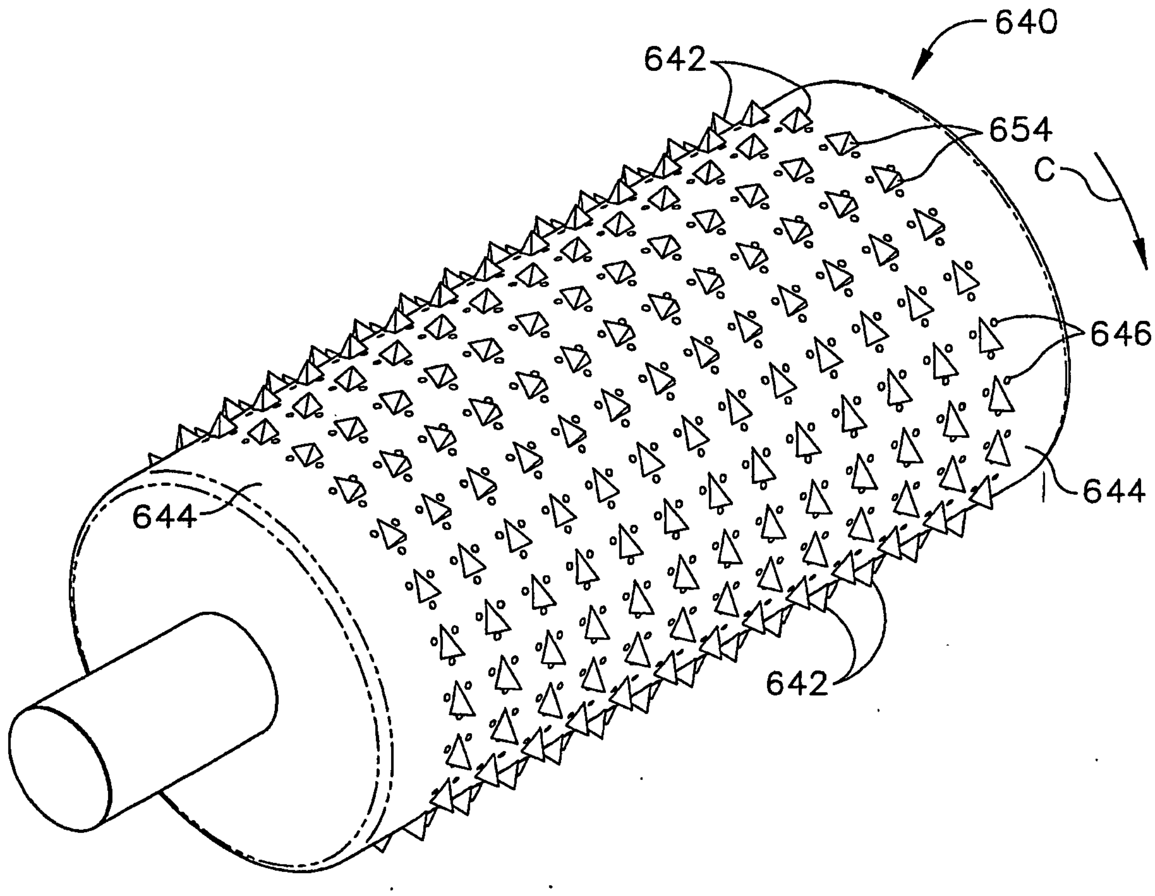


FIG. 38

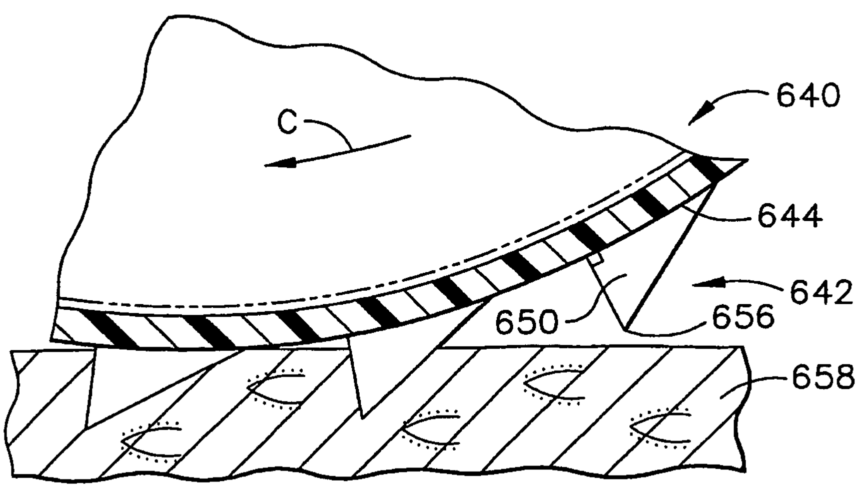


FIG. 39

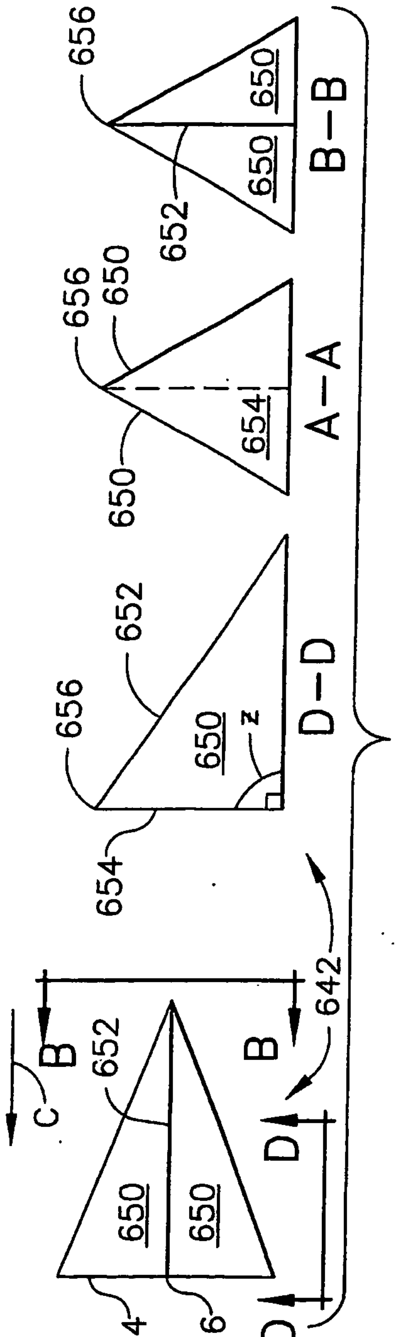


FIG. 40

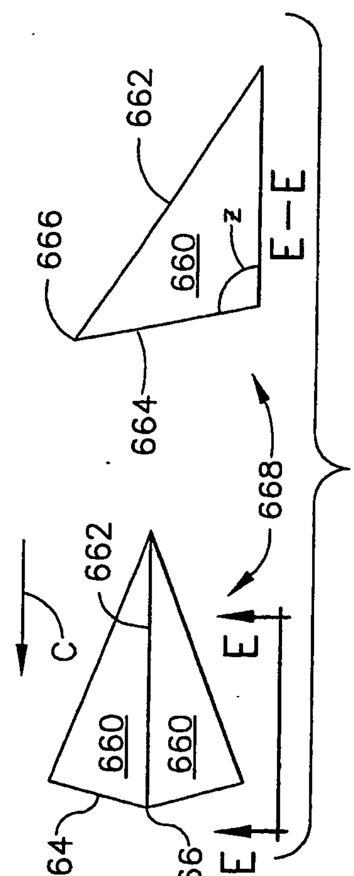


FIG. 41

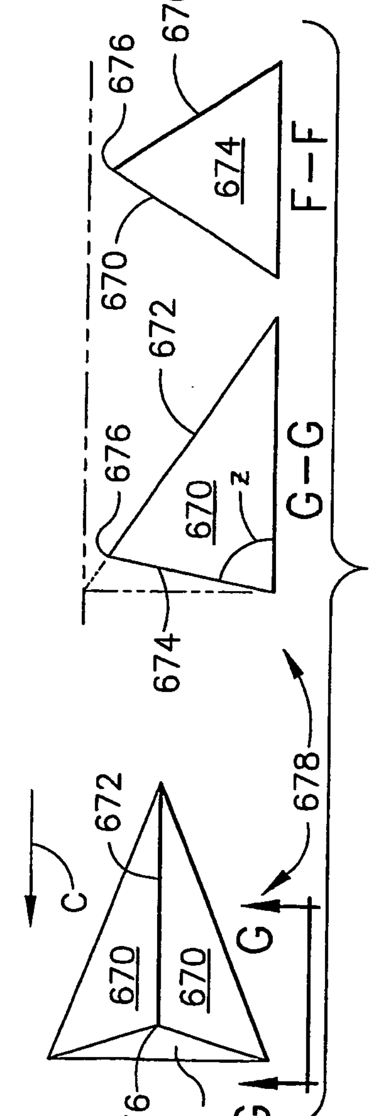


FIG. 42

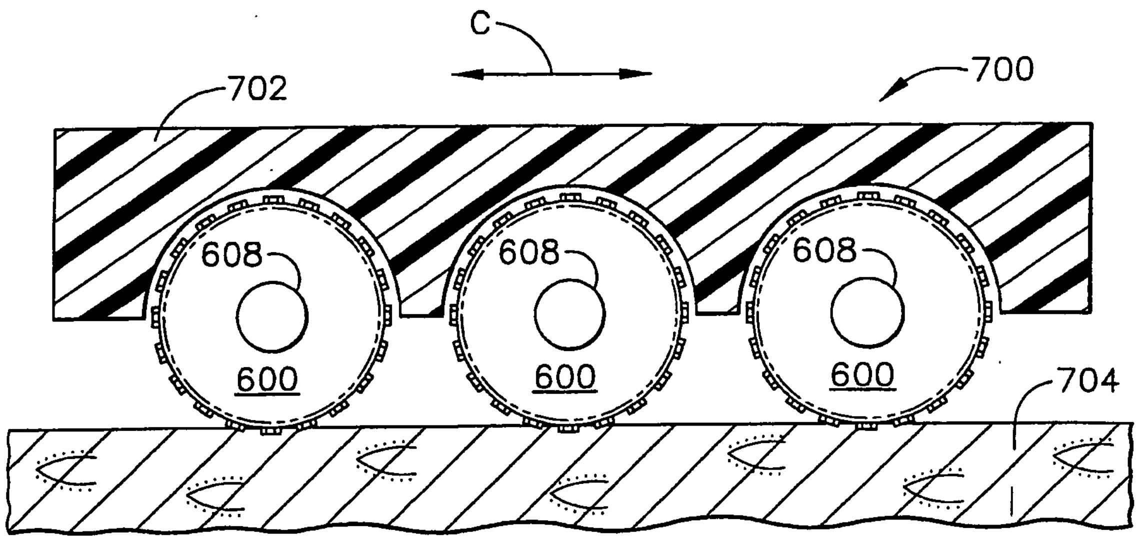


FIG. 43

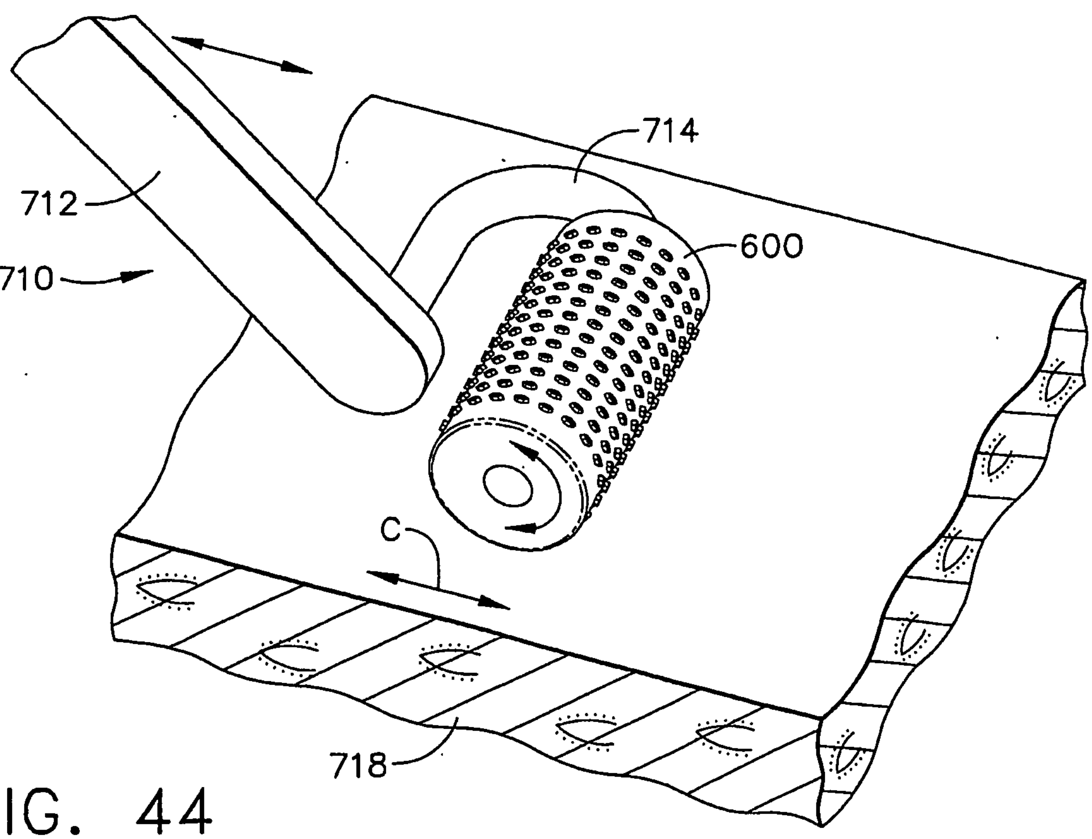
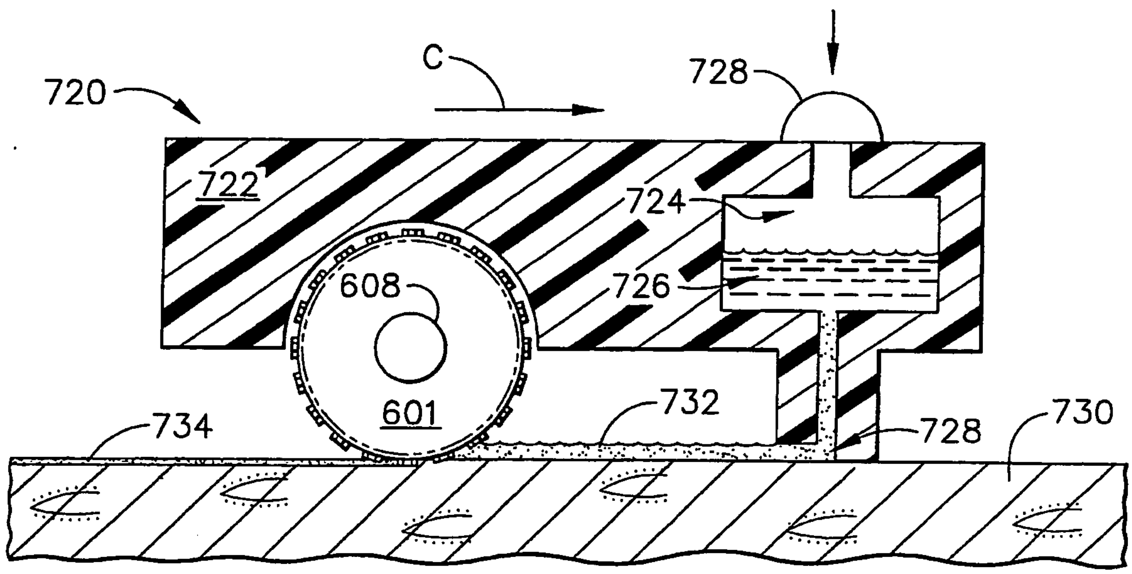


FIG. 44


C
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724
726
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732
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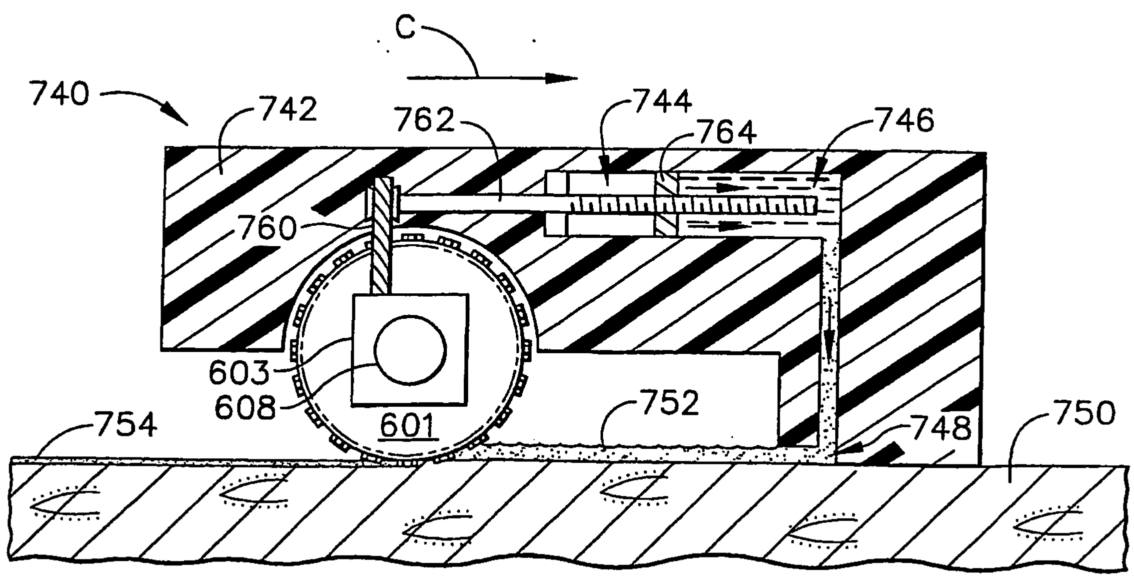
730

FIG. 45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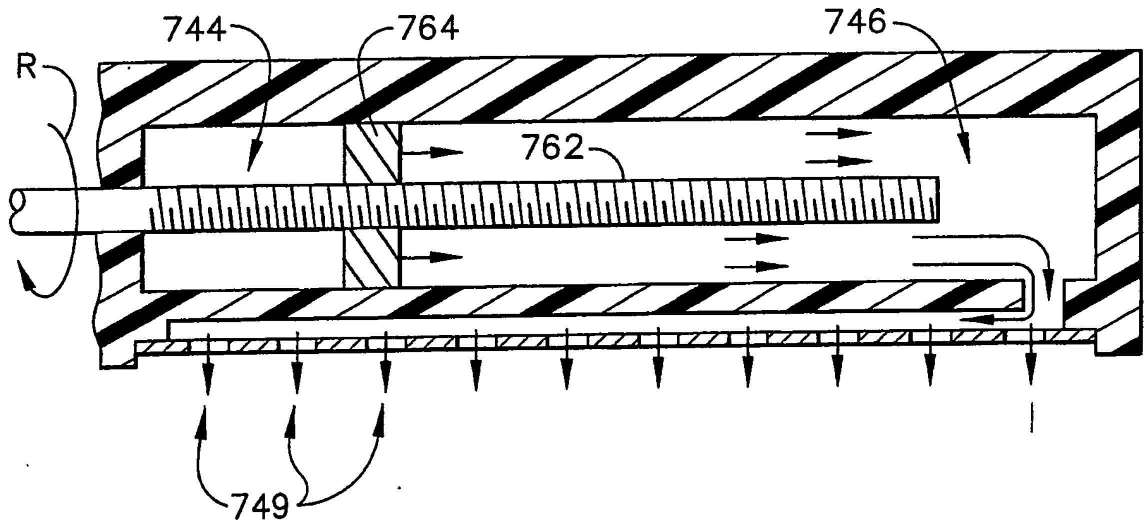
754
748
750

FIG. 46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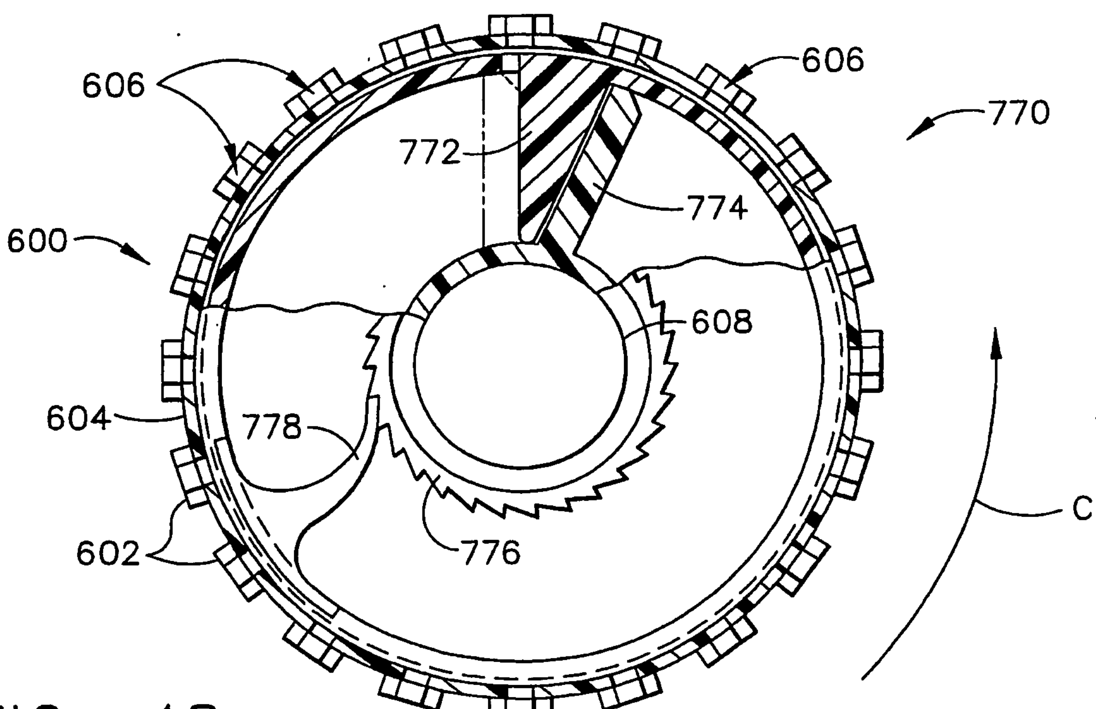
R
762
749

FIG. 47


606
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770
772
774
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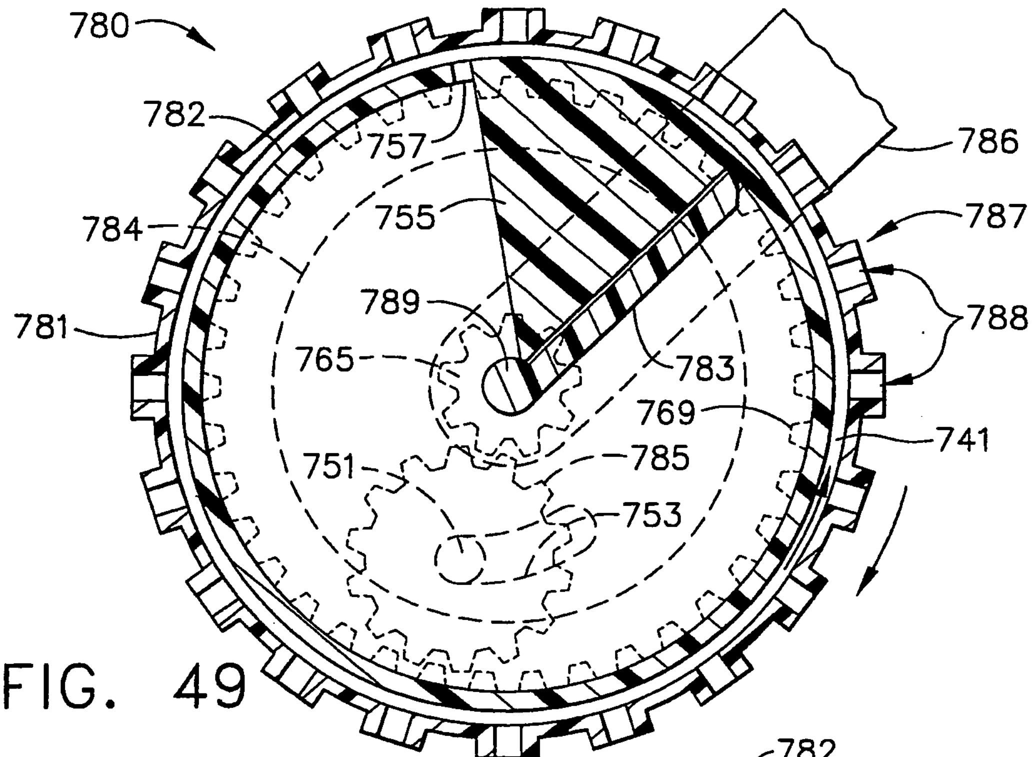
608
604
778
C
602
776

FIG. 48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781
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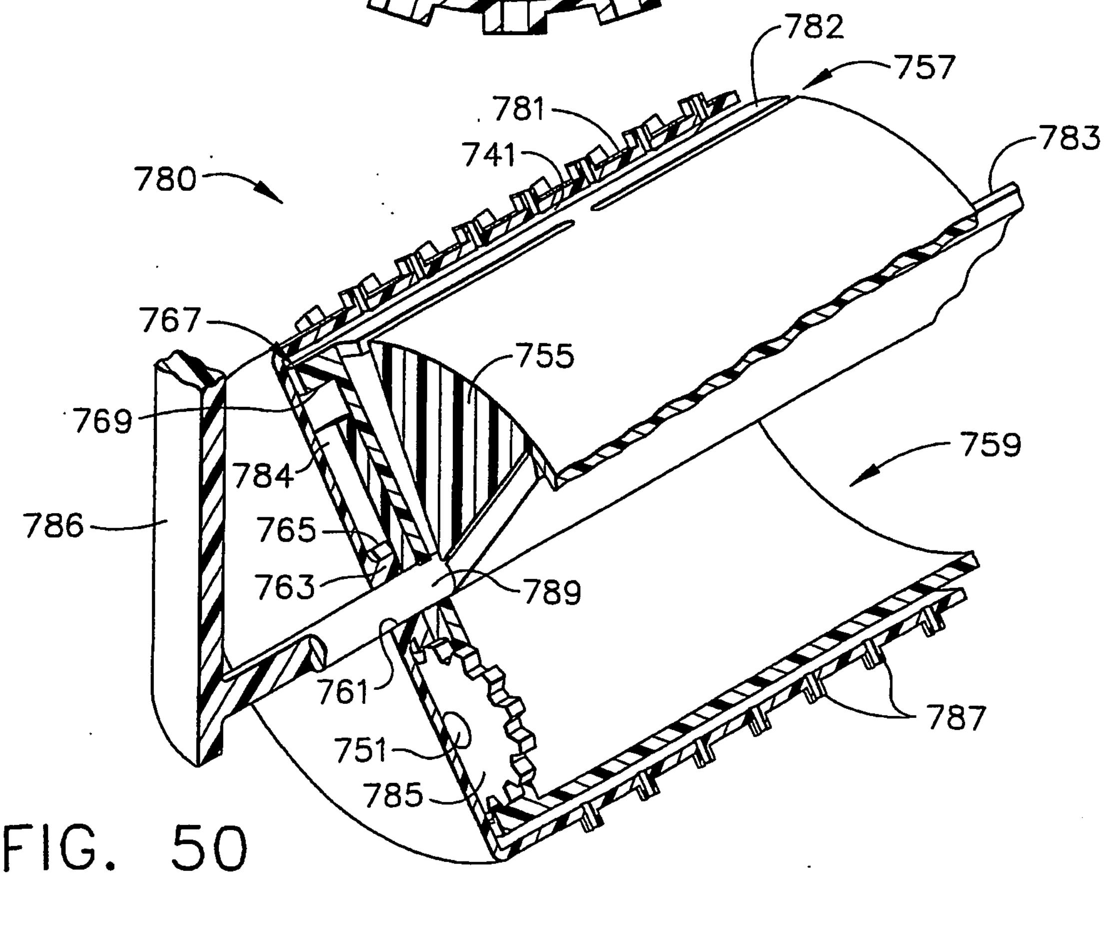
783
769
741
751
785
753

FIG. 49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784
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763
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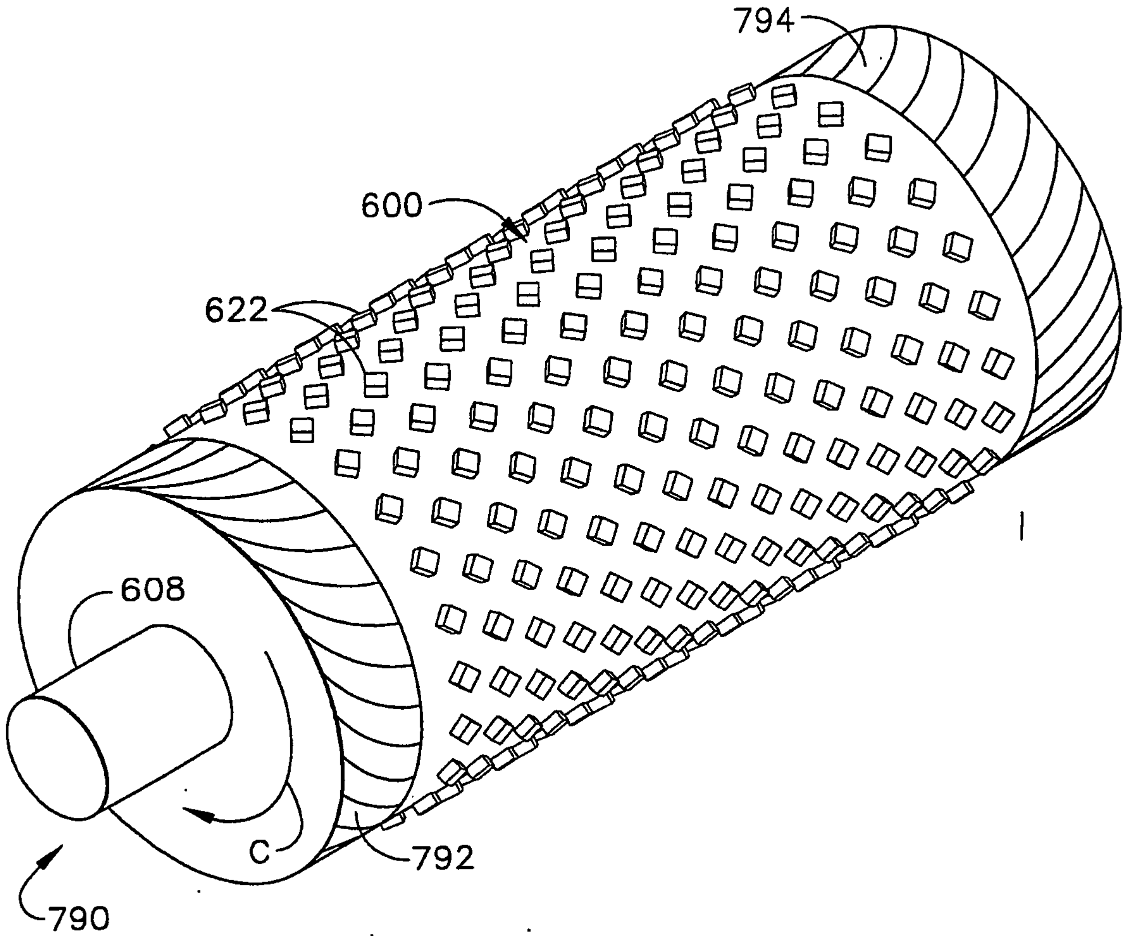
751
785

FIG. 50


794
600
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C
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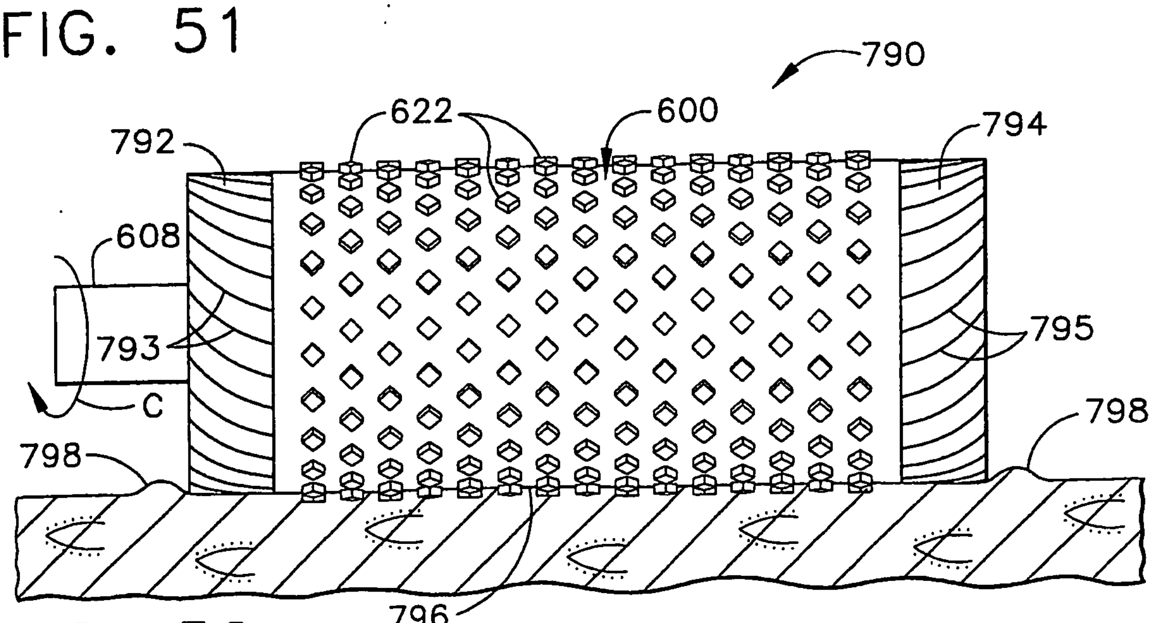
790

FIG. 51


790
622
600
792
794
608
793
795
C
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796

FIG. 52

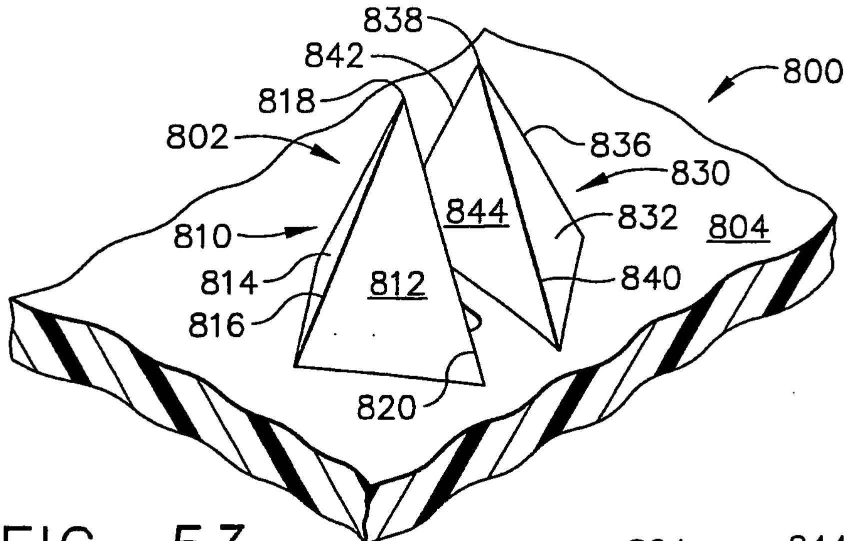

FIG. 53

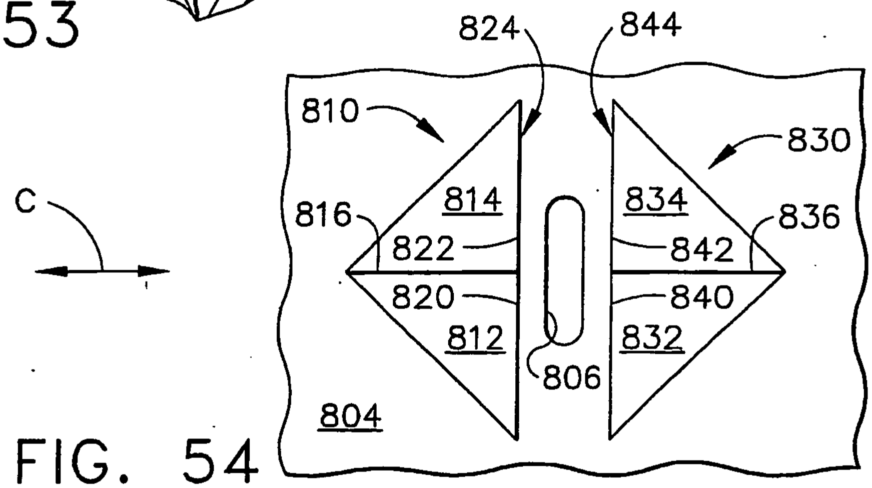

FIG. 54

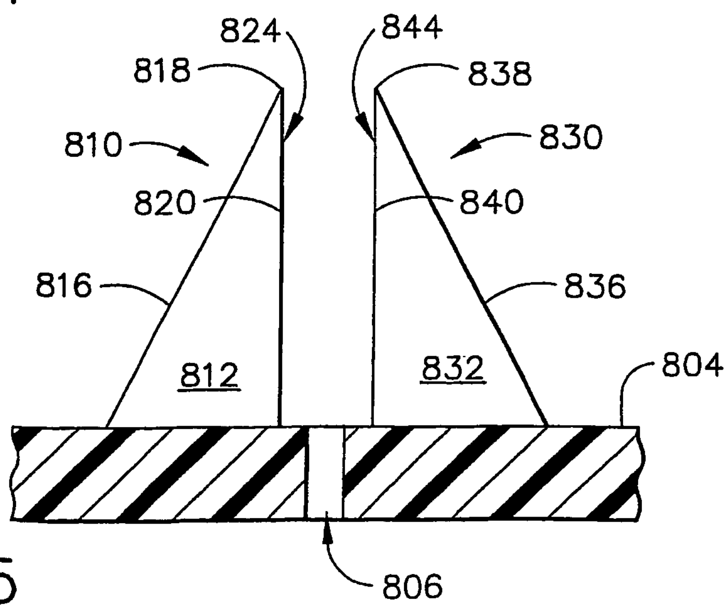

FIG. 55

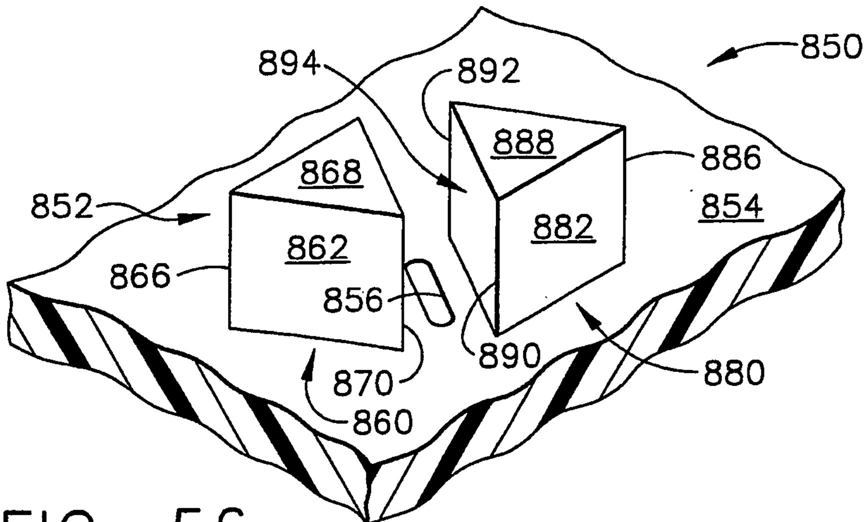

FIG. 56

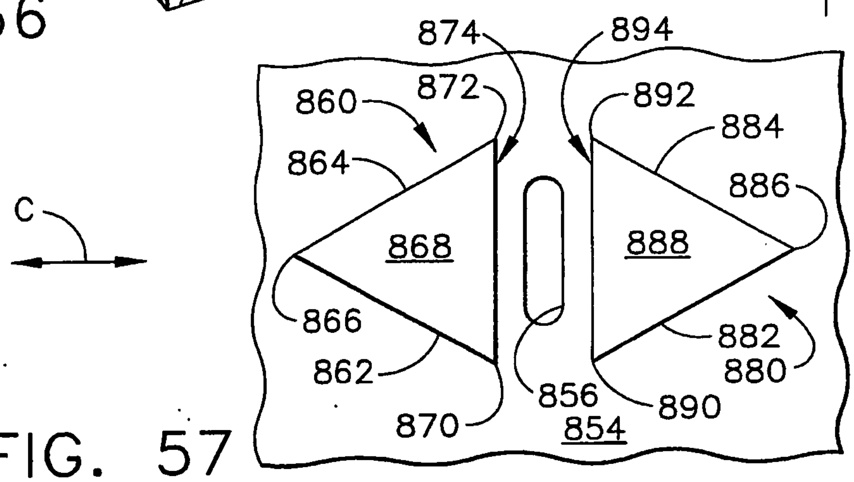

FIG. 57

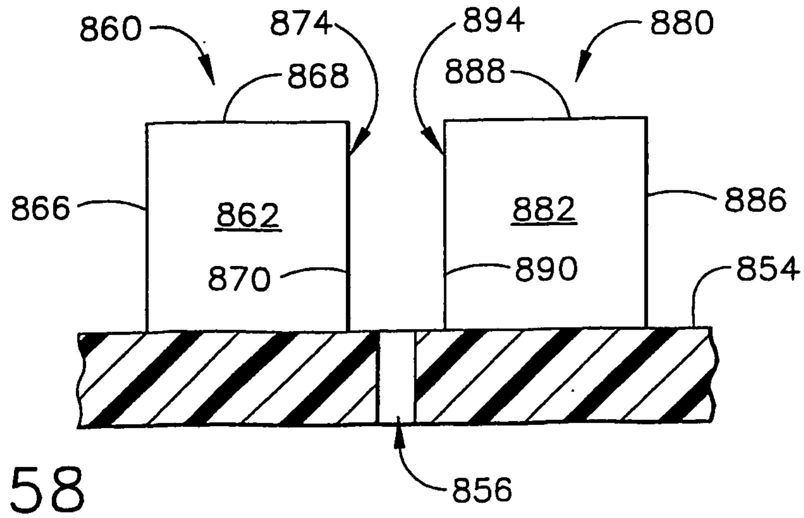

FIG. 58

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